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LIPID PROTEINOSIS (URBACH-WIETHE)

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Though rare, the clinical picture of lipid proteinosis (Urbach-Wiethe disease) presents sufficient characteristics which cannot fail to be observed. Hoarseness and dyspnea due to laryngostenosis led laryngologists, above all, to take interest in the matter.

This subject may be divided into four historical stages. The first refers to former indeterminate observations. Here one may include the case published successively by the laryngologist Siebenmann (1908), by the dermatologist Lutz (1922) and by the anatomopathologist Rössle (1927) with designations of "generalized hyperkeratosis of the skin with involvement of mucosa," "naevus icthyosiformis" and "hereditary progressive pachydermic dystrophy" respectively. In addition to this case, followed for nineteen years by several observers, there is a small group, 3 or 4 cases (1 of these of doubtful retrospective diagnosis), studied by Miescher and later by Nager (1928) under the names "familial keratosis of the skin and mucosae combined with bullous formations and colloidal degeneration of the mucosa" and "congenital dyskeratosis" respectively. In these publications the variability of the designations reveals the inaccuracy of the concepts of the disease. Most of them indicate familial or hereditary influence.

In the second historical stage is included Camillo Wiethe's communication at the meeting in Breslau of the German Society of Otorhinolaryngology in 1924 and the more detailed publication in 1927 of his 6 cases. The lesions were attributed to hyaline degeneration.

In the third stage one has to consider first of all Erich Urbach's paper, presented for publication in November 1928 and published the following year, in which he considered the process as a constitutional disturbance of the lipid metabolism of a nevic nature. He studied 2 cases, previously described by Kerl at a meeting of the Society of Dermatology of Vienna. Next comes the work of Urbach and Wiethe published in 1929, in which, under the title of lipoidosis cutis et mucosae, there was a review of the 6 cases of Wiethe and the 2 of Kerl and Urbach and the inclusion of a new one. In the chapter by Urbach in Jadassohn's *Handbuch* (1932) a minute study of the recent clinical

entity is given. The designation of lipid proteinosis was proposed by Urbach to emphasize his concept that the lesions contain a store of lipidic substance associated with a protidic substance and also to avoid the term lipoidosis, which at the time was assuming too general a character.

The fourth and last stage refers to the cases which have appeared lately and are to be found in table 1. The majority of cases were observed in central Europe, with the exception of 1 case in France, that of Bazex, and of 5 cases in America, those of Tripp, Wise and Rein (2), Montgomery and Havens, and Wile and Snow. Even so, the 2 patients of Wise and Rein were Russian Jews and that of Wile and Snow was a German.

From this historical summary, the importance of Urbach's works, nearly all in collaboration with Wiethe, stands out. These authors were

TABLE 1.—*Cases of Lipid Proteinosis Published up to 1942*

Case	Author	Date	Sex	Age	Observations
1	Urbach and Wiethe.....	1929	M	28	First published by Wiethe (1927)
2			M	27	First published by Wiethe (1927)
3			F	25	First published by Wiethe (1927)
4			F	..	Died in 1923; idem
5			M	24	First published by Wiethe (1927)
6			F	28	First published by Wiethe (1927)
7			F	28	First observed by Kerl
8			F	42	First observed by Kerl
9			F	22	
10	Hoffmann.....	1931	F	28	
11	Benesi.....	1931	M	31	
12	Kindler.....	1932	M	38	Diagnosis to be discussed
13	Urbach and Wiethe.....	1933	M	43	Abortive form
14	Schreus.....	1936	M	23	
15	Tripp.....	1936	M	14	
16	Haxthausen.....	1937	M	..	Probably the same as case 17
17	Hansen.....	1937	M	16	Probably the same as case 16
18	Wise and Rein.....	1938	F	18	
19	Wise and Rein.....	1938	F	5	
20	Bazex.....	1939	M	15	
21	Montgomery and Havens	1939	M	45	Incomplete form
22	Wile and Snow.....	1941	M	62	With amyloidosis

the first to describe in detail the various clinical forms of the new disease and to include it in the group of lesions of the metabolism of lipids.

The eponymic designation proposed by me, after Bazex, of Urbach-Wiethe disease is therefore justified. I do not, however, ignore the value of the work done by pioneers on the subject, especially that of Rössle, the Berlin pathologist. In referring to his early work, he claimed the priority of ascribing the lesions of the Siebenmann-Lutz case to a hereditary alteration of the lipid metabolism. In fact, on page 181 of that work he explained the essential lesions found by admitting an *"ererbte Störung des Stoffwechsels"* ("hereditary disturbance of the metabolism"); and, on page 182, dealing with the discovery of the lipidic deposits, he expressed himself thus:

Die Färbungen auf Fett mit Sudan haben in meinen Präparaten ein merkwürdiges Ergebnis gehabt: während die kranken Epithelschichten der Haut und

der Schleimhäute immer so gut wie vollkommen, meist aber ganz frei von sudanophilen Substanzen waren, funden sich enorme Lipoid ablagerungen in der sklerosierenden Submukosa, etwas veniger in der obersten Cutis.[1]

Rössle's contribution is apparently his discovery, while making a detailed description of the microscopic picture in the Siebenmann-Lutz case, of the sudanophilia of deposits which were formerly interpreted as being of colloidal, hyaline or amyloid nature. Urbach probably made use of this discovery but presented a complete study of the whole question from a clinical, histologic, histochemical and metabolic standpoint, based on several cases, and is thus entitled to undoubted priority in describing the new disease.

CLINICAL DESCRIPTION OF THE DISEASE

Lipid proteinosis is a familial, congenital disturbance, sometimes related to consanguinity, with a possible coincidence with diabetes (or predisposition to diabetes), characterized essentially by a lipidic and protidic thesaurismosis which produces typical lesions of skin and mucosae.

A. Skin.—1. The color of the skin is soiled white or yellowish, like that of wax or old ivory. This tint is diffused but not spread throughout the skin; it predominates wherever there are changes of texture.

2. There is an eruption of punctiform and/or miliary papules which are yellowish white, round, discrete or confluent. Sometimes the papules are so small that they are hardly perceptible, but others, such as appear on the face, nape of the neck and dorsa of the hands and fingers, are well defined (at least this was observed in my case). The papules have no systematic follicular localization. A frequent location of this type of lesion is the margin of the eyelids, where a moniliform arch is formed.

3. Occasionally during the slow evolution of the eruption dark crusts are formed, of variable size, without an inflammatory border and without infiltration of the base. Such lesions are predominant on the face and upper limbs. In spite of the doubt left by Urbach, I am of the opinion that this manifestation may be included as one of the most typical. These crusts, chiefly observed during the primary stage, and therefore noticed in children (reason for omission in the descriptions of fully developed cases), may follow bullous formations as in Bazex'

1. "Staining of my preparations for fat by means of Sudan had a peculiar result: Whereas the diseased epithelial layers of the skin and of the mucous membranes were always nearly entirely free from sudanophil substances, enormous deposits of lipid were found in the submucosa undergoing sclerosis and somewhat smaller ones in the upper part of the cutis."

case, or pustular lesions, as in the first case of Wise and Rein; but from what I have carefully observed, I have the impression that they are the result of necrosis preceded or not by petechial hemorrhagic suffusions of the lipid infiltrations wherever the latter become more evident. Such crusts were visible in the right preauricular region in Hoffmann's case and on the chin in the second case of Wise and Rein. In my case, on two different occasions within a space of two and one-half years I was able to photograph typical lesions of this kind on the face (fig. 5). Removal of crusts shows ulcerations which, after healing, leave scars.

4. The scars are almost pathognomonic. When small and located on the forearms they suggest a papulonecrotic tuberculid. The larger lesions, which are smooth, depressed and atrophic, are similar to those of certain syphilids and also to certain lesions of late yaws. The confluence of these scars combined with the color aforementioned give the skin a characteristic aspect, due partly to the engraved surface and partly to the waxlike substratum on which these engravings are "chiseled." The varioliform scars pointed out by Urbach, but about which he could not decide "whether they have anything to do with the disease in question," were undoubtedly an attenuated form of the lesions that I am describing, and they probably resulted from lesions in evolution which existed in a preceding eruptive stage and, in my opinion, were characterized chiefly by the crusts previously described. These crusts would, in their turn, result from a spontaneous necrosis or maybe from suppuration or some other degenerative mechanism not well defined but of the lipidic or the lipidic and protidic infiltrations proper.

5. In later stages there is a hyperkeratosis, giving the lesions—particularly those on the hands, elbows and knees—a crude verrucoid aspect, which was one of the first lesions observed in completely developed forms of the disease.

B. Mucosa.—Lesions have been observed in the mouth, larynx and pharynx and, exceptionally, on the vulva and in the rectum. These manifestations were first observed by laryngologists, who hold priority in noting this special condition. A constant symptom is hoarseness at an early age, resulting from laryngeal infiltration. On the lips there are lesions on the cutaneous portion, similar to those previously described but forming at times radiating fissures, and also some on the mucous portion, appearing either as diffuse or as nodular infiltrations, forming yellowish white excrescences similar to the cutaneous papules. These elevations form a decided contrast with the vermilion border. The surface of the mucosa may be somewhat rough and present fissures such as those on the lip. These lesions predominate on the lower lip, which becomes rigid from infiltration. Similar but less prominent lesions

occur on the gums, on the floor of the mouth, in the region of the frenum of the tongue, on the soft palate and on the uvula. The tongue, though free from any visible nodular infiltration on the dorsal surface, is often firmer than normal, and its movements are somewhat impaired, which makes its protrusion difficult. The tonsils and neighboring regions, as well as the pharyngeal pillars, often present extensive lesions with enlargement of the tonsil, which contains yellowish nodular infiltrations. These appear on the surface as yellowish dots. At times there is dysphagia which makes the removal of the tonsils necessary, as in my case. The epiglottis and the vocal cords show extensive and deep changes, similar to those described in other sites. These changes produce hoarseness, which is characteristic, and in certain patients symptoms of asphyxia which often demand prompt tracheotomy. The other mucosae seem to be normal, except the vulvar in 1 case (case 9) and the rectal in another (case 17).

C. Hair.—Some authors describe alopecia due to lesions on the scalp. In my case, on the contrary, the hair of the scalp and eyebrows was initially abundant, becoming somewhat sparse as time went on. When there are lipidic infiltrations on the borders of the eyelids, the eyelashes disappear. In men, the beard shows patches of alopecia, which, I think, is due to atrophic scars.

D. Teeth.—A dental anomaly is frequently observed. There is aplasia or hypoplasia, as in my case, of the lateral superior incisors. Since this is generally considered as a stigma of degeneration, it would not be permissible to interpret it as a sign of congenital syphilis in spite of the fact that the Wassermann reaction was positive in my case, as well as in Bazex'. In fact, in most cases the Wassermann reaction has been negative. As far as congenital syphilis is concerned, the classic disturbances of the median incisors have a much greater importance, and in my case these incisors were normal. I thought for a moment of ascribing the positive Wassermann reaction in my case to a disturbance of the lipidic metabolism and to the increase of total lipids in the blood. This interpretation was, however, abandoned almost at once when it was found out that in the majority of the published cases, in spite of a similar metabolic disturbance, the Wassermann reaction was negative. Furthermore, the relative but perceptible improvement of the patient's condition with antisyphilitic treatment speaks here for the high specificity of the Wassermann reaction. In spite of not ascribing the metabolic disturbance directly to the influence of congenital syphilis, one may well accept that when there is concomitance of congenital syphilis and lipoidosis, with or without relationship between the two, the specific treatment may aid, as it did, in improving the cutaneous and general conditions of the patient.

LABORATORY STUDIES

As to skeletal disturbances, nothing in particular has been pointed out by the authors. In the rare cases (the first case of Wise and Rein and the case of Haxthausen and Hansen) in which roentgenograms were made, nothing abnormal was revealed. A roentgen examination is justified, especially of the skull, pelvis and some long bones, when one remembers that in another lipoidosis (Hand-Schüller-Christian disease) multiple lacunar images of the skull bones are observed. Furthermore, infiltration of the bone marrow by cerasin, characteristic also of another

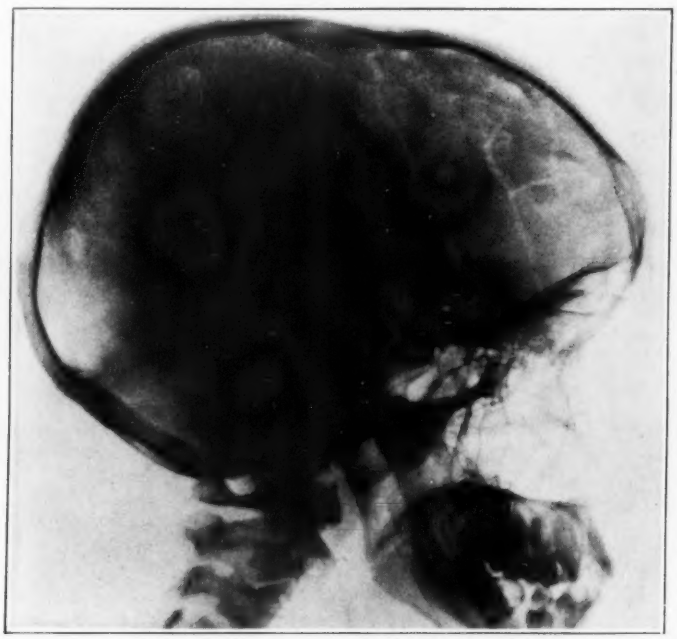

Fig. 1.—Roentgenogram showing folds of dura mater, possibly due to calcification.

lipoidosis (Gaucher's disease), is revealed by an alteration, located preferably on the distal extremity of the femur, which is decalcified and inflated, thus taking the shape of a bottle, according to Snapper's comparison. In my case, which was thoroughly investigated from this point of view with a roentgen examination of the whole skeleton, peculiar formations were found, clearly shown in figure 1. These were located near the posterior clinoid processes and seemed to be difficult of interpretation. They could be considered as calcified folds of the dura mater or even as encysted teeth, as in certain dermoid cysts. Three small

lacunar lesions yet in formation were observed; hardly noticeable, these were round, 5 or 6 mm. in diameter and situated in the region of the vault. Only further observations showing presence or absence of progression may explain the meaning of these small lesions.

Basex' finding of perivascular lipidic infiltrations in an ectopic testicle surgically removed speaks in favor of the concomitant existence of visceral lesions. It is useful to mention here that Urbach a priori considered such deposits when located in the pancreas responsible for the diabetic or prediabetic conditions which may exist in these cases. These deposits would be prejudicial to the normal functioning of the Langerhans islets.

It is frequently observed that more than one member of a family suffers from the disease, and so true is this statement that many of the observations are collective: the K. family (Urbach), the F. family (Wiethe) and the W. family (Wise and Rein). Sometimes reference is made to an ancestor who presented the same manifestations. Hansen verified, by means of a photograph, that his patient's grandmother had had the same disease. The existence, in varying degrees, of disturbances of skin and mucosa in several brothers is less rare. The parents are often consanguineous and, most frequently, first cousins. This was the case in the K. and F. families observed by Urbach and Wiethe and also in my patient. In Tripp's case, the patient's mother and father had latent diabetes. The father and sister in the family studied by Wise and Rein were both free from the disease but showed obesity. All this has only a relative value, given the frequency of these disturbances, particularly in the Jewish race, to which a fair number of observations belong.

Urbach insisted repeatedly on the existence in his patients of either an active or latent diabetes, with basal hyperglycemia or a pathologic blood sugar curve. As has been said, he even went so far as to admit for its pathogenic interpretation that the Langerhans islets of the pancreas were disturbed in their function by the presence of lipid infiltrations similar to those observed in the tonsils. The subsequent reports of cases did not mention the results of the first series. The case published later by Urbach and Wiethe (1933) was normal from this point of view, just as were the cases of Schreus, Hansen, Wise and Rein, and Montgomery, as well as my own case.

As regards the blood lipids, a comparative study of the various observations becomes extremely difficult because of the irregularity of the researches and the variability of methods adopted. Lastly, it must be considered whether the determination was made on the serum or on the plasma.

The normal standards of lipids in the blood in Brazil, as a result of the work done by Gilberto Villela, and in the United States, according to Montgomery and Havens, are as follows:

	Villela	Montgomery and Havens
Total lipids	607 mg.	525 mg.
Fatty acids	350 mg. (total)	345 mg.
Cholesterol	170 mg.	180 mg. (total)
Lecithin	120 mg.	180 mg.

In the cases of Urbach and Wiethe there was a slight increase in cholesterol, a marked increase of "lipid" (lecithin?) and in 1 case an increase of neutral fats. In the following tabulation are given data about the blood constituents in the published cases of lipid proteinosis (Urbach-Wiethe disease), the lipid values being expressed in milligrams per hundred cubic centimeters of plasma.

Benesi:			
Total cholesterol	110	mg.	
Hansen:			
Total lipids	1,250	mg.	
Total cholesterol	251.1	mg.	
Phosphatides as lecithin	482	mg.	
Schreus:			
Cholesterol	125	mg.	
Lecithin	360	mg.	(calculated)
Wise and Rein:			
Total lipids	611	mg.	
Total cholesterol	172	mg.	
Phospholipids	137	mg.	
Bazex:			
Total lipids	575	mg.	
Cholesterol	250	mg.	(in serum)
Lecithin	185	mg.	

Montgomery and Havens:	Feb. 1938	April 1938
Total lipids	552 mg.	470 mg.
Fatty acids	338 mg.	289 mg.
Total cholesterol	214 mg.	181 mg.
Lecithin	181 mg.	258 mg.

Wile and Snow:			
Total lipids (in serum)	691	mg.	
Total cholesterol (in serum)	177	mg.	
Phospholipids (in blood)	220	mg.	
Ramos e Silva:			
Total lipids	1,050	mg.	
Fatty acids	728	mg.	
Total cholesterol	198.4	mg.	
Lecithin	126	mg.	

Only a study of new cases, with repeated determinations always made by the same method, can give any indication worthy of study. Within an interval of two months, the patient of Montgomery and Havens gave entirely different results; it is interesting to notice a compensation between the values of cholesterol and lecithin from one examination to another; while the cholesterol value decreased from 214 to 181 mg., the lecithin value increased from 181 to 258 mg. In my case, as in Hansen's, there was a decided rise of total lipids. Hansen, Schreus, Montgomery and Havens and Wile and Snow observed an increase of lecithin, whereas the values for the other lipids were approximately normal or even low.

As to the chemical analysis of the tissues, the following results were obtained: 1. In the first case of Urbach and Wiethe, Epstein and Lorenz found an abnormally large amount of lecithin in the excised tonsils. 2. In a small piece of hyperkeratotic skin of the finger, Hansen found 1.56 per cent of total lipids and 0.338 per cent of lecithin (less lecithin in the skin than in the blood: 0.338 as compared with 0.482). 3. Montgomery and Havens found slightly higher values for lecithin (1,600 mg. per hundred grams) in the apparently normal skin adjacent to the lesions of the same patient than in the lesions proper (1,500 mg. per hundred grams). There was, however, a decided increase in relation to the normal standards adopted by them: 100 to 900 mg. per hundred grams. 4. In the cases presented by Wile and Snow the determinations made by Eckstein gave practically equivalent values for phospholipids in the blood (220 mg. per hundred cubic centimeters and in the affected skin 240 mg. per hundred grams). There was a certain increase of total lipids in the skin. 5. As there were no available indications here about the lipidic contents of the tissues, I asked Dr. Gilberto Villela to make a comparative analysis of the surgically excised tonsils of the patient (aged 14, white) and those of a normal person of about the same age. A piece of skin with characteristic changes of Urbach-Wiethe disease and an identical portion from the same region of a normal person of the same sex, age and color were analyzed. The results, unfortunately incomplete because of occasional difficulties and as a consequence hardly comparable, are given in table 2.

In no other case was there such a clear demonstration of the enormous increase of phospholipids in the cutaneous lesions, the comparison being made neither with the theoretic averages nor with the apparently normal skin of the patient but with a normal control. The value found for the latter was also high as compared with standards adopted by the American authors, but the difference was considerable, 5.5 Gm. more per hundred grams in our case.

It would be of interest to find out whether by any chance the values for the phospholipids in the control were above the average. But here

one must bear in mind that dead tissues are frequently used for determinations, and in this case the lipidic content may be extremely small as a consequence of wasting diseases which may have led to death. This is a cause of error which may be avoided by the comparative method adopted by me. Besides, the comparison with lower values makes the much increased phospholipid content in my case more evident.

HISTOLOGIC DESCRIPTION

A specimen for biopsy was taken from the posterior cervical region and a second specimen two years later. The tonsils which were excised were also studied.

TABLE 2.—*Comparative Chemical Analysis of the Tonsils and Skin of a Normal Person and of a Patient with Lipid Proteinosis*

	Normal Control	Patient
Tonsils *		
Total weight (wet)	5.10 Gm.	2.82 Gm.
Water content	86 per cent	85 per cent
Cholesterol in 100 Gm. (wet)	175 mg.	180 mg.
Total lipids in 100 Gm. (wet)	880 mg.	1,300 mg.
Skin †		
Weight of pieces analyzed	74 mg.	116 mg.
Water content	72 per cent	71 per cent
Phospholipids	1.1 mg.	8.2 mg.
Phospholipids determined from 100 Gm. (wet)	1.5 Gm.	7.06 Gm.

* The patient's tonsils were divided into two parts, one for chemical analysis and the other for histologic study.

† Specimens for biopsy were taken on the same day from identical regions (posterior cervical region), and the determinations were made immediately; the pieces of skin were not treated with any preservative. Determinations of phosphorus were made by using the reaction of Fiske and Subbarow and photometric determination (Dr. Gilberto Vilella).

A. Epidermis.—The changes were nonspecific. The wavy aspect of the lower limit of the epidermis was preserved, and from it were formed thinner and longer projections. The general structure of the epithelium was maintained regularly with its normal layers, but the pigment was sparse. The mucous layer was free from exudate, and its contents were normal. The granular layer was somewhat variable; in certain regions it had (fig. 2) two or three layers; in others, only a single layer. The keratin formation partly tended to be moderately marked, and small areas of parakeratosis were seen. Nowhere in the epidermis were vacuoles or exudates found.

B. Dermis.—The sections hardened in paraffin showed in the papillary and subjacent layers, beside the normal delicate fibrillar aspect, thicker formations of a hyaline nature. These were of a fawnish rose color in contrast with the rose-red hue shown by normal collagen stained with eosin. Van Gieson's method gave these formations a pale fawnish rose color. The hyaline aspect was observed not only accompanying the capillaries (fig. 2), sometimes adherent to their walls, but

also where no vascular branches existed; and here denser formations were produced which extended either perpendicularly or obliquely to the dermis. These sometimes took other directions and roughly simulated pacchionian bodies and sometimes formed irregular arabesques. Wherever there was a greater development of the lesions there was a decided lessening of nuclei and a hyaline homogeneity, which could be

Fig. 2.—Epidermis with stratum granulosum. The stratum corneum is abnormally dissociated because of technic, frozen sections, compression, etc. In the dermis there are homogeneous hyaline formations directed particularly by the vessels.

compared with amyloid. It must be said here that such similarity is merely morphologic, for in the substance in question the special staining characteristics are lacking. The deeper regions of the dermis were free from these changes with the exception of a few vessels, generally thin, the walls of which showed the same hyaline aspect. A few other vessels, precapillaries and small veins, were surrounded by a discrete

lymphocytic infiltration. The hair follicles were few, which is not surprising, since the patient was adolescent.

The sebaceous glands were normal. The sweat glands, on the contrary, showed a thickening and homogeneity of the basal and collagenous layers of the immediate neighborhood. Broad concentric curves stood out well even with low power magnification. The elastic fibers, which in the deeper regions of the dermis had a normal appearance, were thickened in the upper layers and stained either by Weigert's fuchsin or by orcein with variable intensity and not so uniformly as under normal conditions. Sometimes there was a coincidence between these changes and the presence of lipids, the characteristics of which will be described later.

C. Tonsil.—The general structure of this organ was maintained. In many parts of the corium there were areas with a hyaline aspect either forming homogeneous masses or producing milder changes which involved particularly the vascular walls. In some fields the hyaline bands caused a dissociation of the elements among which they lay. The follicles showed discrete homogeneous fibers, which were not, however, as thick as those of the corium. Although decided changes of this type were found in the tonsil proper, they were also evident in the collagen which separated the lymphoid structure of the tonsil from the neighboring muscular layers and adjacent pharyngeal pillars.

HISTOCHEMICAL STUDIES

Frozen sections of the skin and tonsils were submitted to the different procedures which are recommended for the study of lipids.

Staining with scarlet red showed a substance of lipidic nature which became reddish rose in color and which had the same location as the hyaline homogeneous formations aforementioned (fig. 3). Wherever the coloring was more pronounced, the picture, with an elongated and wavy aspect directed perpendicularly to the epidermis, could be compared with that of flames.

The capillaries, precapillaries and collagen bundles with a concentric disposition around the sweat glands were stained by scarlet red. It must be said that even the sweat glands which were farthest from the involved dermis were here included. This may also be said of the capillaries, some of these, though distant, showing a certain lipidic content. The capillaries of the papillary layer were practically all involved and, consequently, colored red. With high power magnification one could see not only the uniform staining of the vessels and fibers but also delicate granules of red which in certain places seemed to be the only sign of the presence of the lipids. The fattish substance seemed, in a general way, to be incorporated in the hyaline structures, and it did

not present double refraction, as proved by adequate procedures. This substance varied in quantity. As is clearly shown in sections of the tonsil, the greater concentration was almost always found to be in the center of the mass; here the color was stronger, and toward the margins it faded. Neither in the tonsils nor in the skin were xanthelasmatous cells (xanthoma) found.

With sudan III the lipidic masses became reddish yellow, like the color of tile. This shade is intermediary between the *Dunkelorangelbe* obtained by Urbach and the red observed by Bazex when using the same reagent.

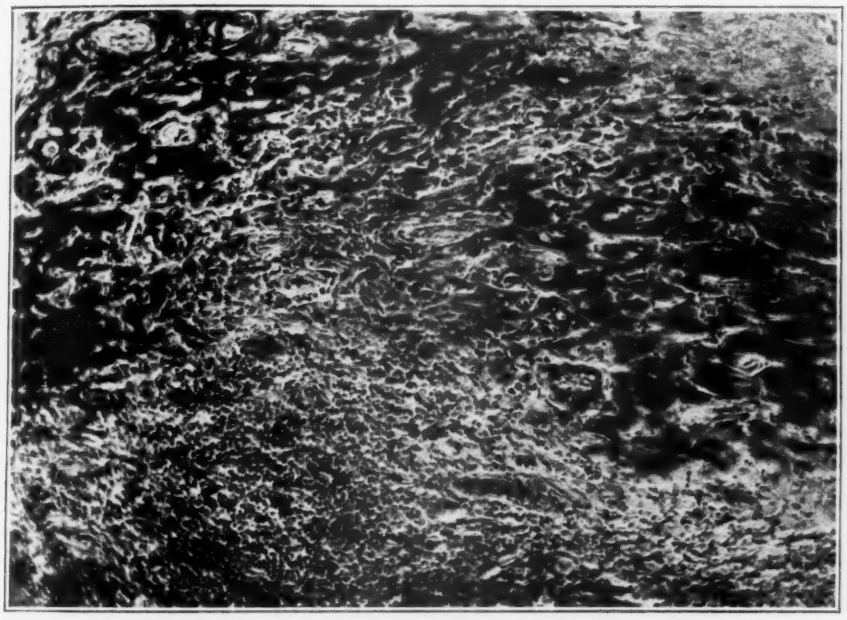

Fig. 3.—A frozen section of tonsil stained by scarlet red and hematoxylin. In the center of the field there are fibers with a hyaline aspect. On the right and left the deep reddish color (black in the photograph) shows that a lipidic substance was incorporated in the fibers.

The nile blue stain gave a violaceous rose color to the sites of greater lipidic concentration and violaceous blue to those of smaller concentration.

The chroming of the sections and the subsequent treatment with hematoxylin, according to Smith-Dietrich's method (fig. 4), gave a blue color of varying intensity ranging from sky blue to Prussian blue. The chroming with chromic acid (instead of the bichromate) proved to be more efficient by giving better coloring and differentiation. The capillaries appeared as blue tubes whose surfaces were sometimes finely

granular. In the keratin layer of the epidermis there was a regular amount of lipids.

The tonsil had a greater quantity of this fattish substance, which was stored here and there and was stained by the reagents that have already been mentioned. It was found under the epithelium, either in the adjacent basal layer as a red band (staining with scarlet red) or

Fig. 4.—Phospholipids in the tonsil stained blue by the Smith-Dietrich method (black in the photograph).

involving uniform and dense formations spread throughout the corium. It is interesting to point out that in the mucosa proper between the cells there was a thin layer of lipidic substance which was observed with every method of staining used and in every section examined. One cannot, therefore, accept this as an artefact. The follicles also showed small bands which were stained with scarlet red. The fibrous portion which separated the tonsil from the adjacent muscles and from

the pharyngeal pillars showed a considerable proportion of lipids and of hyaline tissue. In places where there were considerable quantities of lipidic substance the distribution was not homogeneous. There were fibers which had hardly undergone the hyaline process, particularly the marginal fibers. In others, however, central droplets began to form, which gradually increased in number and which persisted even in the formations which were deeply stained by scarlet red. From what may be observed, especially in the tonsil, there seemed to be first a hyaline transformation of fibers and later the appearance of the lipidic substance. This came as thin droplets and gradually impregnated the whole homogeneous mass.

When treated with solvents of fats this lipid was resistant to boiling acetone for a few minutes, and this was true only for sites of greater abundance of lipids. Absolute alcohol and acetone together dissolved the greater part of these substances, and this fact brought about certain difficulties in the early observations. Seventy per cent alcohol did not act on them, and it is the best solvent for adequate stains such as sudan and scarlet red. The previous chroming of the frozen sections by Ciaccio's method permits the use of absolute alcohol and xylene, since only a minute quantity is dissolved. This can be observed by treating the sections with scarlet red. In the various cases of lipid proteinosis there was a certain variation in the solubility of the lipidic complex, and this may perhaps be explained by the existence of varying degrees of protidic and lipidic combinations, or by quantitative variations of the lipid or lipids in question. It is, however, certain that while Urbach found in his cases insolubility of these substances in cold absolute alcohol, Schreus was able to extract them with some ease with 70 per cent alcohol. Of greater importance here is their solubility in hot acetone. This fact, stressed by Urbach and also observed in my case, distinguishes the lipidic deposits of this disease (soluble deposits) from those of xanthelasmatosis (insoluble deposits).

Summing up, one may conclude from this study that there is an associated or mixed process which seems to consist of a degeneration of the hyaline type, involving thin vascular branches where the degeneration probably begins, the basal layer of the sweat glands and of the epithelium of the tonsil and also the collagen fibers, without any special structural arrangement. Lastly, there is an infiltration, secondary perhaps, of a special lipid. The lipidic substance becomes insoluble by the action of the chrome derivatives (Ciaccio and Smith-Dietrich methods), thus resisting when acted on by strong alcohol and even xylene, which is a powerful solvent. This distinguishes it from the neutral fats. The absence of double refraction differentiates it from cholesterol. The use of other methods, particularly the Smith-Dietrich method, which does not stain the neutral fats, the free cholesterol and the esters of cholesterol

but gives a deep blue color to the phosphatides, shows the affinities of the lipidic substance to the phospholipids, the phosphatides and, perhaps, the lecithin. It is well known that *"non si puo affidarsi ai metodi istochimici per lo studio dei lipidi cutanei"* [2] (Comel), but in lipid proteinosis these histochemical data are confirmed by the chemical analysis itself. In our case the increase of phosphatides in the abnormal skin, as compared with that of a normal person, was absolutely evident. It seems, however, that in spite of this one ought to accept the existence of a simultaneous storage of several substances in the majority of lipoidoses. The verification made by Gilberto Villela (1938) serves as an example. In 100 Gm. (wet) of a "xanthomatous tumor" he found 1.02 Gm. of cholesterol and 2.02 Gm. of phospholipids. These lipidic complexes resulting from true "chemical contaminations," in Fialho's picturesque way of expression, and, moreover, their association with protidic substances which may either exist or not in the abnormal tissues, bring considerable difficulty to the study and interpretation of data gathered from the histochemical and from the analytic chemical studies.

REPORT OF A CASE

M. R. G., a white Portuguese housemaid aged 16, was observed during three years (from November 1937 to November 1940). The data regarding her case were gathered during this time, sometimes with the aid of several colleagues, some of whose names will be mentioned later.

Anamnesis.—The father was living and well; the mother died of yellow fever. They were first cousins. The patient had a younger sister, who was healthy and free from cutaneous manifestations. Besides these two daughters, the mother had had a premature stillbirth and later a child who died at the age of 3 months. The father neither smoked nor drank and had normal skin and a negative Wassermann reaction.

The patient was born after normal pregnancy and labor. She had measles and whooping cough during infancy and later several attacks of influenza. She menstruated for the first time at the age of 14. The cutaneous lesions have appeared since the first years of life, and no information could be obtained as to how they began. From what I could gather, I have the impression that there was a spontaneous appearance of pustules and crusts followed by atrophic yellowish scars. The skin of certain regions, especially that of the face, neck, dorsa of the hands and elbows, gradually became coarse and infiltrated as a consequence of frequent relapses. These regions showed zones of atrophic scars, some with circinate borders, giving a senile aspect to the face. The skin of the face had a special yellowish color, which might be compared with that of old ivory or of wax. The voice had always been somewhat hoarse.

Examination.—The bodily development was poor in relation to her age. The face had a senile aspect due to sequelae of cutaneous lesions. The cutaneous appendages were normal. There were badly implanted saw teeth with hypoplasia

2. "We cannot trust entirely to the histochemical methods for the study of the lipids of the skin."

of the upper lateral incisors (fig. 6), which were later partially destroyed by caries. The median incisors were, on the contrary, normal. There was paleness of the mucosae, and the patient was hoarse.

Fig. 5.—Lipid proteinosis. *A*, Jan. 13, 1937. *B*, April 4, 1940.

Fig. 6.—Hypoplasia of lateral incisor.

The weight was 29.5 Kg. and the height 137 cm. November 1937; the weight was 42.9 Kg. and the height 145 cm. in October 1940.

In October 1940 the secondary sexual characters were normally developed. The hair, abundant up to that time, was now somewhat sparse. The skin of the

regions which were most affected (face, neck, nape and upper limbs) was somewhat thickened and yellowish, like old ivory or the dirty yellow of wax. Now and then one could see whitish or violaceous rose zones of cicatricial atrophy. Here

Fig. 7.—Small miliary granulations, firm and elevated.

and there were small miliary granulations which were firm and elevated, such as were seen on the face, especially on the chin, neck, posterior and upper part of the trunk (fig. 7), dorsal region of the hand (proximal extremity of the thumb) and extensor surface of the right elbow. The rest of the skin was apparently normal except for its general yellowish, or straw, color and a few scars.

This cutaneous picture served as a background for the periodic appearance of lesions with varying aspects: (*a*) petechiae appearing spontaneously and observed only on the face; (*b*) irregular areas with a necrotic aspect, numerous on the face when the patient was seen for the first time; some were slightly circinate, covered by pyohematic crusts (fig. 5) and having an ulcerated surface as base; (*c*) scars left by such lesions, which develop slowly, corresponding to them in shape and size but atrophic and below the normal level, as clearly seen in the posterior region of the elbows (fig. 8); here were small punctiform or lenticular depressions and vast irregular and excavated regions. Lesions of this type were also observed on the extensor surfaces of the knees. The scars were smooth and white, rose-white or lilac-white.

The Nikolsky sign could not be elicited. On the left heel a patch of wine-rose vascular nevus was seen, disseminated along the external border of the foot and slightly over the instep.

Fig. 8.—Scars following disappearance of crusts.

The eyebrows were normal. The hair, which had been quite abundant, was now dry and thin; it began to fall profusely in 1940, having thus become considerably scanty.

The inspection of the mucosa showed the following: (*a*) large numbers of yellowish granulations either isolated or, more frequently, forming continuous patches on the inner surface of the lower lip, soft palate, pharyngeal pillars, tonsils (where they were particularly noticeable and produced a certain degree of dysphagia) and pharynx; (*b*) rigidity of the lower lip, which was sclerosed, and with its mucous portion pale, dry and having vertical fissures and a large number of yellowish granulations especially visible at the bottom of the gingivolabial space; (*c*) similar granulations on the frenum of the tongue (these granulations were not seen on the dorsal surface of tongue, but this organ was, as a whole, somewhat rigid and consistent, thus making movements difficult); (*d*) in the larynx, particularly on the vocal cords, the same yellowish infiltration, which was, however, discrete, and (*e*) normal vulvar mucosa.

Nothing unusual was revealed by the general examination. There was absence of exophthalmos. The urine was diminished in volume. The liver and spleen were normal in size.

In view of the positive Wassermann reaction, injections of a bismuth compound were given. Definite improvement was obtained, with disappearance of the active ulcerated and crusted lesions and persistence of other lesions. There seemed to be a simultaneous stimulus of bodily development, with an increase in weight and height.

As the patient repeatedly complained of a sore throat, the tonsils were removed by Professor Kós.

Some time before the first menstruation there was a recurrence of the necrotic lesions of the face (fig. 5 *B*), but these disappeared rapidly when antisyphilitic treatment was renewed together with oral administration of ovarian extract.

Complementary Findings.—1. Chemical Analysis [3] of the Skin (Determination of Phospholipids):

Phospholipids in 116 mg.	8.20 mg.
Calculated for 100 Gm.	7.06 mg.
Water content	71%

2. Chemical Analysis [4] of a Piece of the Tonsils:

Total weight of the tonsil (wet)	2.8 Gm.
Water content	85.0%
Cholesterol in 100 Gm. (dry)	47.5 mg.
Cholesterol in 100 Gm. (wet)	180 mg.
Total lipids in 100 Gm. (dry)	325.0 mg.
Total lipids in 100 Gm. (wet)	1,300.0 mg.

3. Blood Lipids: [5]

Cholesterol in 100 cc.	198.40 mg.
Fatty acids in 100 cc.	728.00 mg.
Lecithin in 100 cc.	126.00 mg.
Total lipids in 100 cc.	1.05 Gm.

4. Blood Sugar Determinations:

March 21, 1938	1.11 Gm. per liter
Oct. 21, 1940	0.70 Gm. per liter

5. Glycemic Curve, Oct. 21, 1940 (expressed in grams of sugar per liter of blood):

Basal blood sugar content	0.70 Gm.
One-half hour after ingestion of 90 Gm. of dextrose	0.98 Gm.
One hour after ingestion of 90 Gm. of dextrose	1.50 Gm.
Two hours after ingestion of 90 Gm. of dextrose	0.95 Gm.

6. Wassermann Reaction: positive (2 plus).

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3. Determination of the phosphorus was done by the Fiske and Subbarow reaction and photometric determination (Bulletin 607 of Dr. Gilberto Villela of the Instituto Oswaldo Cruz).

4. Determinations were made by Dr. Gilberto Villela (Bulletin 545 from his laboratory, Instituto Oswaldo Cruz).

5. The determinations were made by Dr. Gilberto Villela with the following methods: cholesterol, modification of Bloor's method; fatty acids, method of Himwish, Friedman and Spier; lecithin, Bloor's method with the determination of phosphorus by the technic of Fiske and Subbarow; total lipids, gravimetric method.

7. Basal Metabolic Rate (March 3, 1938):

Standard deviation (Du Bois modification)	+ 11%
Standard deviation forty minutes after ingestion of 50 Gm. of ham	+ 52%
Specific dynamic coefficient	+ 41%

8. Urinalysis (Sept. 12, 1940):

Volume in twenty-four hours	650 cc.
Specific gravity	1.027
Sugar, fats and double refracting lipids	None

9. Roentgen Examination (Aug. 30, 1940): The lungs, heart and aorta were normal. The inspection of the whole skeleton did not reveal any abnormality other than the following: The hypophysial fossa (sella turcica) was normal, but the clinoid process showed two zones of calcification with the shape of "angel wings," with a backward and outward direction, which might possibly be calcified folds of the dura mater (or dental formation of a dermoid cyst?). These formations were about 1 cm. in length and were localized by the stereoroentgenographic examination. In addition, the cranium showed three lacunar regions, which were hardly perceptible.

10. Ophthalmologic Examination: The fundus and the perimetry were normal.

11. Histologic Examination (March 19, 1938; Dr. Amadeu Fialho): The epidermic disturbances in the piece of skin examined were slight: There were slight hyperkeratosis and small areas of parakeratosis. In the dermis there were thick formations with a hyaline aspect, involving the capillaries, precapillaries and the basal layer of sweat glands. These formations might represent either mild or evident disturbances according to their volume. Such lesions predominated just below the dermic papillae. Staining by scarlet red and by sudan III, especially when dissolved in 70 per cent alcohol, showed a refracting lipidic substance which included the homogeneous formations already described. Xanthelasmatous cells were not found.

Summary.—A girl, the daughter of cousins, was observed from 1937 through 1940 (11 to 14 years of age). Ever since her first period of infancy, the skin showed yellowish white elevations, diffuse waxy yellow infiltrations, crusty necrotic lesions and atrophic scars; the mucosa showed sclerosis and yellow granulations limiting the movements of the lips and tongue and causing dysphagia and hoarseness. There was a positive Wassermann reaction, with improvement following antisyphilitic treatment. The roentgenographic findings in the cranium have not yet been described in lipid proteinosis (Urbach-Wiethe disease). There was a considerable increase in the phospholipids of the skin.

DIFFERENTIAL DIAGNOSIS

The association of congenital disturbances, mucous and cutaneous lesions and hoarseness forms a characteristic syndrome which may be clinically diagnosed, as in our case. A biopsy will confirm the clinical impression; an examination of the paraffin sections shows the structure mentioned elsewhere and the absence of foam cells. Frozen sections show an absence of double refracting crystals and the existence of a

substance with affinity for the sudan stain. This substance is found in the dermis in general and around the vessels in particular.

1. *Epidermolysis Bullosa Hereditaria.*—This disease bears the greatest resemblance to lipid proteinosis in spite of being totally different in its essence. It is congenital and rare, with mucous and cutaneous lesions. The lesions are sometimes of the bullous type, as in certain cases of lipid proteinosis, and whitish epidermic cysts with scars, etc., are observed. The dystrophic form is serious and may be mistaken for the disease under discussion. The presence of two characteristic elements of lipid proteinosis would be enough to differentiate one condition from the other. These characteristics are the hoarseness and yellow-white papules; these differ from the epidermic cysts, which are similar to the granulations of milium. On the other hand, the histologic structure differs entirely, and in epidermolysis bullosa the lipidic deposits are absent.

2. *Hydroa Vacciniforme.*—In Bazin's hydroa vacciniforme there are bullous lesions which leave scars and sometimes deformities of the ears, nose and hands. These lesions are produced through the influence of light on the skin, which is sensitized by porphyrins. This disease could hardly be mistaken for lipid proteinosis.

3. *Atrophoderma Vermiculare.*—This disease, which affects the face, called also atrophoderma reticulatum and folliculitis ulerythematosa reticulata, is not as grave as lipid proteinosis. The lesions are symmetric and localized on the cheeks, forming thin designs with atrophic depressions, each of which corresponds to a follicular ostium. Histologically there is slight atrophy of the epidermis, sometimes accompanied by a limited basophilic atrophy of the collagen.

4. *Symmetric Adenoma Sebaceum.*—The aspects of the two types of symmetric adenoma sebaceum are entirely different. Their principal location on the sides of the nose, the absence of mucous disturbances and of lesions on the extremities, their tumor-like nature and their characteristic histologic structure will prevent any confusion between the two diseases. The only point of contact is the fact that they are both genodermatoses.

5. *Pseudoxanthoma Elasticum.*—This is essentially a degenerative state of the elastic dermal tissue, whose fibers undergo a change which was described by Darier for the first time as elastorrhexis. Clinically, the lesions are predominant on the trunk and in the articular folds and appear as discrete yellowish or cream-colored areas, sometimes slightly elevated; often there is a coincidence of visual disturbances (chorioretinitis). There are neither mucous lesions nor degenerative stigmas. The lipidic deposits observed in lipid proteinosis are absent here.

6. *Colloid Milium.*—I presented a case of this well known condition in collaboration with Fialho in 1933. The plaques, confluent translucid elevations, containing a colloid, are located on the exposed parts of the body and form a special clinical entity which can be histologically confirmed.

7. *Hyaline and Amyloid Degenerations.*—This condition may be confused with lipid proteinosis. As has already been said, the latter disease was first described by otorhinolaryngologists as being hyaline degenerations. According to Rössle's observation, the diagnosis may be made by selective stains for lipids, such as those of the sudan type. As regards the cutaneous lesions, amyloid lichen differs entirely in its aspect, location and staining reactions (metachromasia), as was seen in my paper on this subject (1940). Until now, in only 1 case, that of Udo J. Wile, presented as an instance of disseminated amyloidosis at a joint meeting of the societies of dermatology of Chicago and Detroit in 1940 (and later reported in full by Wile and Snow), were amyloidosis and lipid proteinosis shown to coexist. This led to the conclusion that "the fact that amyloid was also present in our case seems to indicate that these two syndromes may overlap in certain respects."

8. *Xanthelasmatosis.*—Certain forms of xanthelasmatosis may invade the mucosae, thus making it more difficult to establish a different diagnosis with lipid proteinosis and much more so when it is considered that analogous disturbances of the lipidic and glucidic metabolism may coexist in both cases. Besides the clinical characteristics which have been given in detail, the diagnosis of lipid proteinosis will find support from the following items: (*a*) absence of foam cells, characteristic of xanthelasma; (*b*) absence of double refracting lipids (beware of possible existence, pointed out by Urbach, of the cholesterol cysts of the tonsils); (*c*) presence of abundant extracellular deposits of lipids with special morphology and stained electively by the specific methods for phospholipids, as, for example, that of Smith-Dietrich, and (*d*) the chemical analysis, showing increase of phospholipids in the lesions.

9. *Hand-Schüller-Christian Syndrome.*—The characteristic triad of the Hand-Schüller-Christian syndrome (exophthalmia, diabetes insipidus and multiple lacunar images of the cranial bones) and the granulomatous structure of the lesions in which foam cells are still found will permit an early differentiation.

10. *Necrobiosis Lipoidica.*—Recent works compel me to discuss the differential diagnosis between lipid proteinosis and necrobiosis lipoidica; each of these may or may not be associated with diabetes, and the lipidic deposits are not extracellular. Foam cells are absent. In necrobiosis, cholesterol is the lipid increased, especially in its free form, but there may be a considerable increase in lecithin. The clinical picture is, how-

ever, different. The lesions predominate on the lower limbs, and lesions of mucous membranes are absent. Histologically, there are vascular disturbances which form the characteristics of necrobiosis.

11. *Miscellaneous.*—In lipid proteinosis there is no enlargement of the liver and spleen, and this fact separates it easily from visceral lipoidosis and from the syndromes of Niemann-Pick, Gaucher, Bürger and Grütz. The statement is particularly applied to the last-mentioned syndrome, in which the cutaneous involvement is manifest.

SUMMARY AND CONCLUSIONS

A. Lipid proteinosis (Urbach-Wiethe disease) is a typical condition well defined from the clinical, histologic and chemical standpoints.

1. Clinically it forms a syndrome, the components of which are: (*a*) a polymorphous eruption composed simultaneously or successively of yellowish papules, hyperkeratotic plaques, small hemorrhagic effusions, pyohematic crusts, ulcerations and atrophic scars; the predominance of lesions on the face is typical, resulting from multiple designs having a dirty yellow color as background; (*b*) mucous lesions, principally of the mouth, pharynx and larynx, having the same aspect of yellowish white infiltrations and presenting, because of their location, special symptoms, such as rigidity of the tongue, dysphagia, hoarseness and eventually severe dyspnea; (*c*) dystrophies of different kinds and sometimes disturbance of the dextrolipidic metabolism.

2. Histologically, forming a band around the vessels and in the dermis is found a substance which is colored in varying shades by the sudan stain and scarlet red. This substance differs from common fats.

3. Histochemically and chemically this substance is a lipid belonging to the group of phospholipids and intimately united with a protein.

B. Lipid proteinosis may be studied from three different angles: as a disturbance of the lipidic metabolism, which is of special interest to the internist; as a lesion which may cause serious symptoms of the larynx and demand the help of a specialist, and, lastly, as a mucous and cutaneous disturbance of interest to the dermatologists who described this new pathologic entity.

C. I am of the opinion that the disease may be well defined in three ways: (1) as a genodermatosis, nevoid disturbance, familial disease, often related to consanguinity (in a certain number of cases, including my own, the patient was the child of first cousins; besides the incidence of the disease in several descendants, there are nearly always other stigmas of degeneration, for instance, dental anomalies, such as aplasia of the lateral incisors, and weak bodily development); (2) as a thesaurismosis, with storage in the corium of certain mucosae, in the dermis and around the vessels, of a special substance probably deriving from a

disturbance of the lipidic metabolism (according to Von Gierke's conception [1931], the disease may be placed in a natural nosologic family); (3) as a lipoidosis, since the histochemical examination and the chemical analysis of the substance in question prove it to be a phospholipid (this disease would thus present a greater similarity to Bürger-Grütz and Niemann-Pick syndromes, which are also phosphatidoses, than to the xanthelasmatoses, which are essentially cholesteroses).

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AN UNUSUAL VARIANT OF EPIDERMOLYSIS BULLOSA

RECURRENT BULLOUS ERUPTION OF THE FEET

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A patient was presented before the Dermatological Section of the Royal Society of Medicine by Weber [1] with an unusual bullous condition involving the feet that occurred only during warm weather. The case was presented under the title "Recurrent Bullous Eruption on the Feet of a Child." No dystrophies of the appendages were noted, nor did any scarring, atrophy or milia appear following the healing of a lesion. Weber suggested that the condition might be a mild atypical form of epidermolysis bullosa. Sequeira, in discussing this presentation, indicated that he had never seen epidermolysis bullosa limited to the feet, the lesions always being much more generalized.

The eruption in Weber's case affected only 1 member of a family. On the other hand, Cockayne,[2] in 1938, reported the existence of this condition in two family groups under the term "Recurrent Bullous Eruption of the Feet." He observed 3 members in one family with this and on investigation found that there were 3 others occurring in four generations of the same family. In the other family group 12 instances were demonstrated occurring in five generations. Descent in every case was direct. Cockayne stated that "since we only know the condition in the heterozygous state and do not know whether it would be the same, more severe or even lethal in the homozygous state, it must be called, following Levit's nomenclature, a conditional dominant." He felt that since the disease was so rare it was not impossible that the two families he reported were connected, although no direct proof was available.

Although this disease is found particularly on the feet, in Weber's case there was a history of a single bullous lesion that had been present on the perineum. In 1 case of Cockayne's group there was a history

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1. Weber, F. P.: Recurrent Bullous Eruption on the Feet of a Child, Proc. Roy. Soc. Med. (Sect. Dermat.) **19**:72, 1926.

2. Cockayne, E. A.: Recurrent Bullous Eruption of the Feet, Brit. J. Dermat. **50**:358 (July) 1938.

of lesions appearing on the palms after the patient played golf, although it was stated that the patient believed these lesions to be ordinary blisters.

In the patients reported on by both Weber and Cockayne the bullous lesions appeared consistently only during warm weather. Cane[3] reported on 3 patients with epidermolysis bullosa in the same family. In these also the dermatosis was worse in warm, moist weather. Although many lesions appeared on the feet of these patients, there were also bullae on the shins, the backs of the hands and at other sites of trauma. Milia and scarring were definite sequelae observed, in contrast to the absence of these changes in the patients of Weber and Cockayne. The latter pointed out that Cane's patients were affected with the dystrophic type of epidermolysis bullosa and were not to be grouped with his patients.

In Weber's patient and in Cockayne's group the dermatosis appeared in every instance during the first or second year of life. Although the patients were incapacitated by the condition, at no time was it a cause of death.

The following case is an instance of a dermatosis similar to that just described and represents the third family group to be reported in the literature.

REPORT OF A CASE

M. L. R., a white man aged 20, a soldier, was seen for the first time on May 26, 1941, for a bullous condition of the feet. The patient volunteered the information that blisters appeared on his feet only during warm weather, this condition having been reappearing since infancy. Although lesions appeared predominantly on the plantar surfaces and the sides of the feet, on a few occasions blisters appeared on the palms following such manual labor as working with an axe or a shovel. Once, five years ago, four large vesicles appeared on the back of the neck, which he attributed to wearing a starched collar; also, on one occasion several years ago the patient had a transient bulla on each knee. When the temperature was low no bullae appeared regardless of how much activity the patient was engaged in and regardless of the month of the year. The appearance of lesions elsewhere than on the feet was most unusual, and the history of such occurrences was obtained only after constant questioning over a period of two months.

The patient stated that as soon as bullae appeared he was compelled to reduce his activity and spend most of his time in bed. He found that simple rupture of the lesions was all that was needed to assure rapid healing. No scars or changes in the skin resulted. After being ruptured, the bullae healed in four to seven days. The lesions ranged from 1 to 2 cm. in diameter.

Past History.—Other than the usual childhood diseases and an occasional infection of the upper respiratory tract the patient's past history is essentially irrelevant.

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3. Cane, L. B.: Epidermolysis Bullosa: Three Cases, with History of the Disease in Four Generations of the Same Family, Brit. M. J. **1**:1114, 1909.

Family History.—The patient's grandfather had a similar disease. The grandfather had 5 offspring (fig. 1), 3 of whom, 1 male and 2 females, had the identical dermatosis (a male and a female being spared). The affected aunt gave birth to 4 children, of whom 2 males and 1 female were involved and 1 male was not affected. The uncle had 1 offspring who had this dermatosis; no history was available as to the number or the fate of his other children. The third affected member of the grandfather's offspring (the patient's mother) had 9 children, 5 males and 4 females, of whom 4 and 1, respectively, had this disease. The patient's sister who has this dermatosis has had 4 children, 2 of whom have this dermatosis. Two of his involved brothers have had 6 and 1 offspring each, of whom 3 and 1, respectively, are similarly affected. The remaining brother and the patient have had no children.

In most of the affected members of the patient's family the dermatosis involved only the feet and appeared only during warm weather. Occasionally a member of the family had lesions on the palms following manual labor during warm weather, and only 1 member (the patient's brother) gave a history of having a lesion on any other site than the feet and hands, a bulla having appeared on

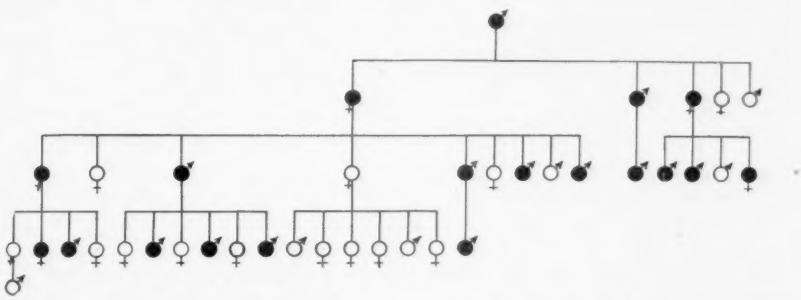

Fig. 1.—This diagram indicates the incidence of the dermatosis in four generations of the family of the patient reported on (the black circles indicate affected members of the family).

the neck once following the wearing of an excessively starched collar. No unaffected member of the family has had a child with this condition. Each involved person first had the lesions in infancy, while he was still of crib age. It was felt by the family that the babies acquired bullae from kicking the bed clothes and the sides of the crib. No member of the family group had any scars or sequelae resulting from lesions. The family had no other developmental defects and appeared to be of good average intelligence, with no unusual character traits.

Examination.—The patient presented approximately twelve bullae on the plantar surface and on the side of each foot and one large lesion on each hallux. The area surrounding the fresher bullae was not inflamed. Slight areolas of erythema were seen about the older lesions, which appeared to be secondarily infected. The roof of each bulla was thick. The newer lesions contained a straw-colored fluid, and the older lesions were filled with a turbid, milky material. Between the toes of both feet there was a very slight scaling. Because of this observation and before adequate significance was placed on the patient's history a preliminary diagnosis of dermatophytosis and bullous dermatophytid was made by the referring physician.

The results of the rest of the physical examination were essentially normal.

Laboratory Findings.—Examination of the urine gave negative results on several occasions. The reactions to two Kahn tests for syphilis were negative. Examinations of the toes for fungi gave negative results, as did also examination of the stool for parasites and ova. Examination of the blood gave the following results: white blood cells 9,650, red blood cells 4,330,000, hemoglobin 65 per cent and a differential count of 64 per cent polymorphonuclear leukocytes, of which 3 per cent were eosinophilic cells, 33 per cent lymphocytes, 2 per cent monocytes and 1 per cent myelocytes.

Treatment and Course.—The summit of each bulla was excised, and the patient was then given foot baths of 1:5,000 potassium permanganate solution every four hours; once daily each lesion was painted with 2 per cent alcoholic solution of gentian violet. In five days the lesions had healed completely, and the patient was discharged from the hospital.

Two hours after leaving the hospital, after walking about casually, the patient stated that blisters reappeared. He was readmitted to the hospital three days later, at which time a fresh outbreak of bullae was noted. He was given the same type of therapy and experienced the same rapid healing of the lesions.

After being kept in bed for seventeen days, during which time no new lesions had appeared, he was permitted to walk about the ward for ten hours to see if this minimal trauma would be responsible for an outbreak. The following morning twelve new bullae were observed on both feet, ranging in size from 1 to 2 cm.

Microscopic Examination.—An entire bulla was excised from the outer surface of the right foot for microscopic examination. The specimen was studied by two different laboratories.

The following report was received from the Army Medical Museum:[4] "The section of skin 7 mm. long and 2 mm. deep exhibited moderate hyperkeratosis, slight acanthosis with fusion and clubbing of the rete pegs, spongiosis and occasional hydropic degeneration of the rete cells. The main feature of this section was a bulla 5 mm. long separating the epidermis from the dermis. The bulla contained recent hemorrhage, hyperemia and slight perivascular round cell infiltration involving the superficial dermal blood vessels (fig. 2). The diagnosis was epidermolysis bullosa."

From the laboratory of Drs. D. L. Satenstein and W. Sachs the report of "typical epidermolysis bullosa" was obtained.

Elastic tissue was normal in distribution and character (Weigert's stain).

With the Wright stain of the contents of a new bulla there were revealed a few red blood cells, an occasional degenerated epithelial cell and a white blood cell count of 14 per cent lymphocytes, 18 per cent polymorphonuclear leukocytes and 68 per cent eosinophils. One white cell was found in every ten to fifteen high power fields.

Continued Observations.—An attempt was made on several occasions to produce lesions by rubbing various areas vigorously with the thumb for three minutes continuously. Three areas were selected, the plantar surface of the right foot, the outer surface of the right foot and the chest. No lesions were produced on the plantar surface of the foot or on the chest; however, bullae appeared regularly on the sides of the foot following this type of trauma. Nikolsky's sign was not elicited on any part of the body.

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4. The microscopic preparation and photomicrograph were prepared at the United States Army Medical Museum, Washington, D. C. (negative no. 71864).

COMMENT

This case report is of interest in view of the apparent rarity of this type of dermatosis. The history and observations on this patient are similar to those described by Weber and Cockayne. Only after persistent history taking over a two month period was information obtained as to the existence of lesions on sites other than the feet. One of Cockayne's patients gave a history of unusual blisters on the palms, and Weber's patient had a lesion in the perineum as well as on the feet. The

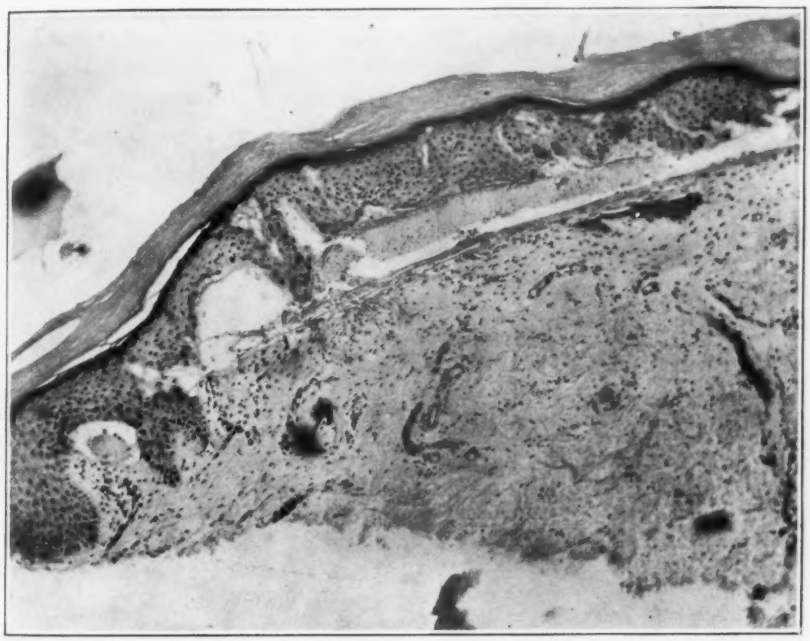

Fig. 2.—Photomicrograph (× 74) of a bulla excised from the right foot, indicating the subepidermal location.

constant appearance of lesions only in warm weather and the predominance of lesions on the feet seem to identify this disease.

Weber observed that lesions could not be produced artificially by rubbing. On the other hand, little difficulty was experienced in producing lesions by rubbing the sides of the feet of the patient described herein. No success was obtained in artificially inducing lesions on the plantar surface of the feet, also a predisposed site, and on the chest, where lesions have never appeared. The failure to produce lesions artificially on the soles may be due to the normal thickness of the skin at this site. This might also be explained by the inability to simulate artificially the type of trauma required to produce lesions. The constant

history that lesions appear on the feet only when the patient is not confined to his bed and the demonstration of this fact in the case presented would suggest a traumatic effect. The reappearance of lesions following casual walking about a hospital ward for ten hours implies that trauma must be a responsible factor. That the trauma seems to differ from the direct type of trauma usually responsible for epidermolysis bullosa seems to be evident but does not in itself make this a separate entity.

In total, 19 members of the patient's family were affected, of whom 14 were males and 5 females. For a clearer picture of the familial and sex distribution, the patient's family tree was studied, with elimination

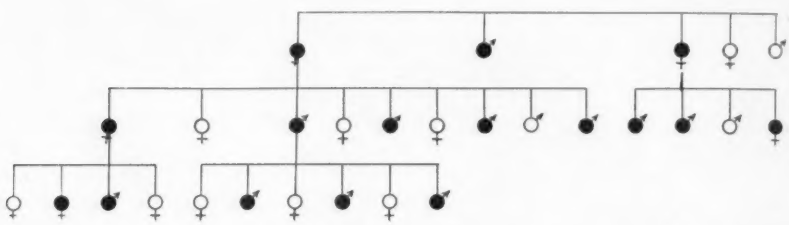

Fig. 3.—This diagram indicates the familial incidence of the dermatosis in the family group of the patient reported on, with incomplete sibships eliminated.

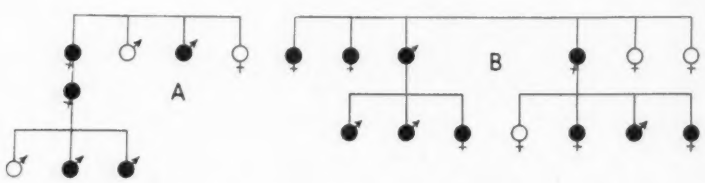

Fig. 4.—This diagram indicates the incidence of the dermatosis in the two family groups (*A* and *B*) reported by Cockayne, with incomplete sibships eliminated.

of all portions in which knowledge of complete sibships was lacking and in which the individual parents were too young to have had their complete family expectancy (fig. 3). In this group there were 28 persons, 16 of whom had this disease (57 per cent). Eleven out of a total of 14 males are involved, and only 5 of 14 females. Cockayne's data treated in the same manner (fig. 4) show that 15 out of 21 members of the two families had this disease, an incidence of 71 per cent as compared to 57 per cent in the present series. Comparison of the relationship of sex shows 7 males and 8 females in Cockayne's series, as compared with 11 and 5 respectively in this study. Analysis of the sex incidence between the two series shows some similarity: occurrence in 7 of 9 males in Cockayne's series as compared with 11 of 14 in this report, and among

the females, 8 of 12, as compared with 5 of 14. However, the numbers are too small to draw conclusions.

Cockayne,[5] in analyzing the ratio of affected to normal siblings in a large series of typical epidermolysis bullosa found it to be 201 : 163, an incidence of 55 per cent, of whom 59 per cent were males and 41 per cent females. These figures roughly parallel those obtained in the present series (incidence of 57 per cent, with 69 per cent males and 31 per cent females).

The similarity of the hereditary and sex incidence, and the identity of the pathologic findings with epidermolysis bullosa together with the demonstration here of a definite trauma effect, places this condition in the same group as epidermolysis bullosa. It is superfluous to regard this dermatosis, with its peculiar symptomatology, as a distinct entity removed from epidermolysis bullosa. That this is an unusual variant of epidermolysis bullosa should be emphasized, rather than that it is a separate dermatosis, as implied by the nomenclature given to it by Cockayne and Weber.

It is apparent that a dominant type of heredity indicates the occurrence of this disease. However, if it were a pure dominant the incidence would be 1 : 1 (50 per cent). The predominance of affected members of the families in Cockayne's group and the present series (57 per cent and 71 per cent respectively) suggests that this dominant is conditioned by other factors as yet not understood.

It is of interest to compare this disease with a bullous dermatosis recently described by various authors under the following names: vesicular variant of keratosis follicularis (Darier) (Pels and Goodman[6]), familial benign chronic pemphigus (Hailey and Hailey[7]), recurrent herpetiform dermatitis repens (Ayres and Anderson[8]) and dyskeratoid dermatosis (Frank and Rein[9]).

Frank and Rein suggested that the disease described by them and the other authors is probably most closely related to epidermolysis bullosa. The dermatosis herein described presents another deviation

5. Cockayne, E. A.: Inherited Abnormalities of the Skin and Its Appendages, New York, Oxford University Press, 1933, p. 122.

6. Pels, I. R., and Goodman, H. H.: Criteria for the Histologic Diagnosis of Keratosis Follicularis (Darier): Report of a Case with Vesiculation, Arch. Dermat. & Syph. **39**:438-455 (March) 1939.

7. Hailey, Howard, and Hailey, Hugh: Familial Benign Chronic Pemphigus, Arch. Dermat. & Syph. **39**:679-685 (April) 1939.

8. Ayres, S., Jr., and Anderson, N. P.: Recurrent Herpetiform Dermatitis Repens, Arch. Dermat. & Syph. **40**:402-413 (Sept.) 1939.

9. Frank, S. B., and Rein, C. R.: Dyskeratoid Dermatosis, Arch. Dermat. & Syph. **45**:129-151 (Jan.) 1942.

from the usual picture of epidermolysis bullosa. It is interesting to conjecture the possible number of variants epidermolysis bullosa may present.

SUMMARY

This is a report of an unusual hereditary bullous dermatosis that appears predominantly on the feet only in warm weather and leaves no sequelae.

Study of the familial incidence in four generations reveals that this occurs as a conditioned dominant characteristic.

Evidence indicates that this is an unusual clinical variant of epidermolysis bullosa and should not be identified as a distinct entity.

Valuable aid in acquiring the family history was obtained from the family's physician, Dr. J. W. Potts, Easley, S. C.

XCIV. MINERAL CHANGES IN NEURODERMATITIS REVEALED BY MICROINCINERATION

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AND

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Chronic disseminated neurodermatitis is apparently characterized by a cutaneous deficiency of magnesium, as has been determined previously [1] by spectrographic analysis. Evidently, the whole skin of patients suffering from this disorder either is incapable of absorbing biologically essential amounts of this element or loses its capacity for retention of already absorbed magnesium. The unaffected skin of patients with neurodermatitis is histologically different from skin of healthy persons in that the epidermis is acanthotic, hyperkeratotic and hyperpigmented.[2] In unaffected skin the dermis is densely packed with long ropelike cords of connective tissue fibers of a collagenous nature. It is significant that the entire skin of patients with neurodermatitis is measurably thicker and obviously tougher than that of normal persons. The thickening and hardening are due in part to an increase in fibrous elements in the dermis. Such fibrosis is especially marked prior to the development and after the healing of a lesion. The primary reaction in the development of a lesion in this disease appears to be a physicochemical change in the spinous cells by which the nuclear constituents adsorb acid fuchsin less intensely, the nucleoli become heavily keratinized and the cytoplasm is deeply colored with aniline blue (a dye having a strong affinity for collagenic substances).[2] The problem is to determine the mineralization

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Dr. E. V. Cowdry directed the senior author in the cytologic study. Dr. Gordon H. Scott placed his laboratory at our disposal.

Studies, observations and reports from the Dermatological Department of the Barnard Free Skin and Cancer Hospital and the Anatomical Laboratory, Washington University School of Medicine.

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1. MacCardle, R. C.; Engman, M. F., Jr., and Engman, M. F.: Spectrographic Analysis of Neurodermatitic Lesions, Arch. Dermat. & Syph. **44**:429 (Sept.) 1941.

2. MacCardle, R. C.; Engman, M. F., Jr., and Engman, M. F.: Histology of Neurodermatitis, Arch. Dermat. & Syph. **44**:161 (Aug.) 1941.

of the various strata of diseased and of normal skin and to localize the initial mineral changes in the primary lesions.

By microincineration one can accomplish the removal of all organic substances—a troublesome factor in the demonstration of inorganic salts by histochemical technics—thus reducing the metallic salts of proteins and inorganic substances to their simplest form for chemical and physical analysis of the total mineral constituents—those combined with protein molecules and those free as electrolytes—of tissues and cells in the same topographic relationship as existed in the fixed tissue and perhaps closely comparable to the state of distribution obtaining in living tissue.

The recognition of a few individual elements in incinerated sections is not difficult. Calcium and magnesium are present in the form of oxides which appear under dark field illumination as a white ash. Iron is oxidized to form a red or yellowish iron oxide easily distinguishable from any other mineral residue. Silicon appears as a glittering white gold-colored ash that is doubly refractive under polarized light. Sodium and potassium are not as accurately identifiable, although it is believed by some investigators that all of these two elements in a tissue appears as a bluish ash. Although magnesium is not distinguishable from calcium in incinerated sections because the ash residues of both of these elements are white, in specimens which are heavily laden with this white ash of calcium and magnesium and whose spectrograms show large amounts of calcium and but little magnesium, it is reasonable to assume that the bulk of the white ash is calcium and not magnesium. But it is not safe to assume a lack of magnesium in any particular layer of skin unless that layer be devoid of white ash and magnesium be lacking in the spectrogram. Kruszynski [3] stated that he was able to detect magnesium by precipitation with sodium phosphate, but this reagent will also precipitate calcium readily. The recognition of magnesium in the presence of calcium in incinerated sections is not feasible unless the tissue is first subjected to spectrographic analysis.[4] Hence, a study was undertaken of microincinerated sections of specimens of skin from the same 33 patients with neurodermatitis whose histologic features and spectrographic analyses have been described elsewhere.[5]

In 1930 Gans [6] used the microincineration technic of Schultz-Brauns [7] for a histotopochemical study of calcium ash in 22 specimens

3. Kruszynski, J.: Cytochemische Untersuchungen der Veraschten Nervenzelle, Bull. Internat. Acad. polon. d. sc. et d. lett., Cl. méd. **2**:105, 1934.

4. Scott, G. H.: A Critical Study and Review of the Method of Microincineration, Protoplasma **20**:133, 1933.

5. MacCardle, Engman and Engman (footnotes 1 and 2).

6. Gans, O.: Zur Histo-Topochemie der gesunden und kranken Haut, Arch. f. Dermat. u. Syph. **161**:607, 1930.

7. Schultz-Brauns, O.: Die Methode der Schnittveraschung unfixierter tierischer Gewebe, Ztschr. f. wissensch. Mikr. **48**:161, 1931.

of normal and of diseased skin of persons of varying ages and found that in normal skin the deposition of calcium is greatest in the cornified layer and the stratum germinativum and that there are certain regional variations. Rivelloni [8] also found regional differences in the total amount of ash in the epidermis of biopsy specimens of skin taken from patients of different ages. He described sex and age differences as well. Rivelloni studied 25 cases which he divided into five different groups according to age and sex of the patients, thus allowing a limited number to each group. It should be pointed out that the Schultz-Brauns method, which Rivelloni used, involves certain disadvantageous features. In the first place, the technic of freezing and cutting with a cold knife on the ordinary freezing microtome and subsequently incinerating without dehydration at lower temperatures would of course tend to cause dissolution of tissue minerals in the water on heating and probably during freezing. On the other hand, sections cannot easily be cut at a uniform thickness and thin enough to permit estimation of intracellular ash. Meltzer and Kühtz [9] used this method to study chronic inflammation of the skin and found that this condition is characterized by a local cutaneous magnesium deficiency, while an acute fresh inflammation shows an accumulation of magnesium.

Scott,[10] using his own modification of Policard's technic,[11] observed that when incinerated sections of human skin are immersed in distilled water and examined after drying, the white ash of the cytoplasm is decreased in amount while the nuclear ash is almost as dense as before the treatment. He concluded that the calcium and magnesium content of the nucleus is greater than that of the cytoplasm. Scott also reported from a study of embryonic and adult epidermis of a large number of different kinds of animals, including man, that there is a curious reversal of mineralization from embryo to adult. Whereas in embryonic epidermis there is little white ash of calcium and magnesium and much of potassium and sodium in the outer layers, in adult epidermis these layers leave dense deposits of white ash after incineration. The same investigator further called attention to his significant observation that scattered irregularly about in the germinative layer are cells in which the nuclei show considerable amounts of intranuclear iron while their immediate neighbors contain little of this element. Such cells, he stated,

8. Rivelloni, G.: Richerche spodografiche in cute umana normale, Gior. ital. di dermat. e sif. **16**:1, 1938.

9. Meltzer, H., and Kühtz, E. H.: Ueber den Einfluss der Röntgenstrahlung auf das anorganische Gewebegerust der Haut, Strahlentherapie **62**:406, 1938.

10. Scott, G. H.: The Localization of Mineral Salts in Cells of Some Mammalian Tissues by Microincineration, Am. J. Anat. **53**:243, 1933.

11. Policard, A.: Sur une mèthode de microincinération applicable aux récherches histochemiques, Bull. Soc. chim. biol. **33**:1551, 1923.

are not associated with pigmentation. Kooyman [12] studied, using Scott's method, several sections of human skin from the abdomen of a Negro. He extracted the sections before incineration and found that much of the white ash could be dissolved out or redistributed by tiny droplets of water or other solvent.

Horning [13] described the ash of incinerated normal human skin and stated that the apparent heavy mineralization of the basal cell layer as compared with the sparsely mineralized superficial strata is an illusion due to crowded nuclei in the basal cells. Cathie,[14] in a study of the nuclear inorganic substances in normal and in cancerous skin, stated that there is an actual increase in the ash content of the basal cells over that of superficially located cells. However, Cathie mounted sections in distilled water before incineration, which procedure, as Kooyman [12] had shown, could easily modify the distribution of the ash residue.

MATERIAL AND METHODS

Specimens of skin from 171 healthy and diseased persons were studied by microincineration according to the technic of Scott.[10] By a judicious comparison of ashed sections of these tissues with their spectrograms,[1] it was possible to obtain a qualitative and a relatively accurate quantitative estimate of the minerals in the topographic arrangement existing originally in vivo.

For comparison with diseased skin, we first estimated the minerals in 83 specimens of skin taken from normal persons varying in age from infancy to 91 years. Specimens of skin from 33 patients with chronic disseminated neurodermatitis were taken chiefly from the cubital fossae and popliteal regions, where active lesions prevailed. Most of the specimens from active lesions were accompanied by specimens of unaffected skin, and specimens from healed lesions (that had previously been studied during active stages) from the same patients were also obtained.

As further controls specimens from patients with several other inflammatory cutaneous diseases were similarly studied. The number and distribution of these specimens as to age of the patient and region of the body, as well as the technical procedure employed in biopsy, were given in our recent papers on the spectrographic analysis [1] and the histology [2] of neurodermatitis lesions.

One half of each specimen was prepared for microincineration and histologic examination and the other for spectrographic analysis (previously reported). One portion of each was fixed for twenty-four hours in a mixture of 9 parts of dehydrated alcohol and 1 part of 40 per cent neutralized solution of formaldehyde, dehydrated in dehydrated alcohol for three hours, cleared in xylene for three hours

12. Kooyman, D. J.: State and Localization of Inorganic Salts in the Skin as Revealed by Extraction and Micro-Incineration, Arch. Dermat. & Syph. **32**:394 (Sept.) 1935.

13. Horning, E. S.: The Action of Radium on the Inorganic Structure of Tumor Cells as Shown by Microincineration, Scient. Rep. Invest. Imp. Cancer Research Fund **11**:67, 1934.

14. Cathie, J. B.: Inorganic Nuclear Content as an Index of Tumor Radiosensitivity, J. Path. & Bact. **48**:1, 1940.

and embedded in paraffin. Sections cut 5 and 6 microns thick were mounted dry and incinerated in a quartz tube oven at 600 C. for thirty minutes. Sections adjacent to the incinerated ones were stained by Masson's trichrome method[15] and with hematoxylin and eosin. Sections of normal and of diseased skin were mounted in most instances on the same slide to make the comparison more direct. Other portions of the specimen were fixed in Zenker's solution (prepared with solution of formaldehyde), Regaud's fluid and sometimes Bouin's fluid; the histologic observations have been reported elsewhere.[2]

In making the photomicrographs the exposure times for films and prints and the developing fluids were kept as nearly uniform as possible.

NORMAL HUMAN SKIN

The mineral content of normal human skin as revealed by microincineration varies with age. To strengthen the comparison, we describe specimens from the cubital fossa, popliteal region, neck and abdominal and thoracic regions of patients varying in age from birth to 50 years. These include 70 of our 83 specimens, as listed elsewhere.[2] It will be noted that only 1 of our patients with neurodermatitis was beyond 40 years of age. The changes in mineral content after the age of 50 will be described only briefly and under a separate heading. There are no significant regional differences in the ash of the epidermis or dermis proper of our specimens of human skin, although the cutaneous appendages, such as hair and glandular structures, exhibit regional differences which do not seem to bear much pertinent value in this discussion and will be described in a later paper.

Infant Skins.—In epidermis taken from healthy infants less than 1 year old the corneum leaves a bluish residue possibly indicative of the presence of potassium or sodium or both (fig. 1 *A*). Here and there in the corneum there are thin streaks of fine granules of white ash of calcium and magnesium, none of which is doubly refractive (silicon). The granular cells leave a bluish ash also, and their nuclei are almost devoid of ash. The nuclear membranes of the granular cells are sharply defined by thin layers of white (calcium and magnesium) and yellowish (iron) granules of ash. Neither the keratohyalin granules nor the intercellular fibrils leave any mineral residue by which their boundaries can be delimited. It is to be noted here that in the stained (Masson) preparations of these young skins the corneum is not heavily keratinized and the intercellular fibrils and keratohyalin granules in the stratum granulosum are faintly stained with ponceau xylidine (a dye which has a strong affinity for keratin). There are no large nucleoli in the granular cells, and those small ones present leave no definable ash and are not heavily stained with ponceau xylidine.

15. Masson, P.: Carcinoids and Nerve Hyperplasia of the Appendicular Mucosa, Am. J. Path. **4**:181, 1928.

Because of the marked difference in staining capacity of the corneum and keratohyalin granules between faintly colored young and heavily colored adult skin, it is doubtful whether the horny constituents of the corneum in young skin represent true keratin. No comparative chemical analyses of young and of adult keratin are available in the literature on keratin at the present writing. It is also pertinent to

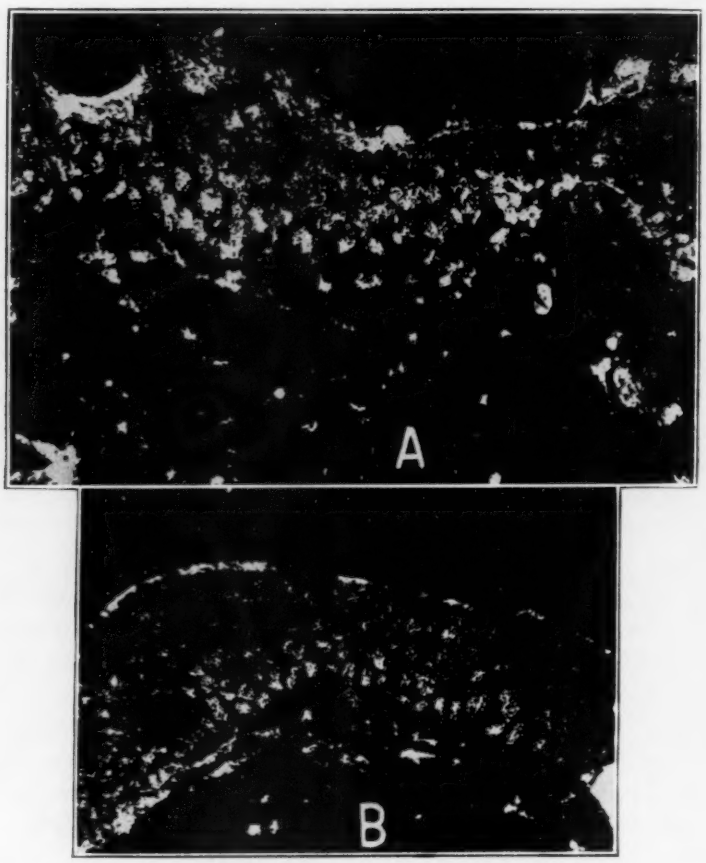

Fig. 1.—Normal infant skin (× 900). *A*, infant less than 1 year old. Note lack of white ash in outer layers. Corneum leaves little white ash of calcium and magnesium.

point out here that not only are the corneum and intercellular fibrils poorly keratinized in young skin but also there is little if any demonstrable pigment in the basal cells.

The spinous cells of infant (less than 1 year) epidermis differ conspicuously in ash content from cell to cell. The outermost prickle cells, nearest the stratum granulosum, leave for the most part a deep bluish

ash (indicative of the presence of sodium and potassium), while the deeper prickle cells, toward the basal layer, are packed with dense masses of white ash of calcium and magnesium. One cell may be almost free of white ash while its neighbors may contain dense deposits of it (fig. 1 *A*). In histologic preparations it is easy to identify these ash-poor bluish cells of the incinerated sections, not only by use of the comparison ocular on the microscope but also by observation of their less intensely stained protoplasm. It may be said that in general cells which contain these dense deposits of white ash of calcium and magnesium will be found to color more intensely with acid fuchsin and other dyes than do cells which lack white ash. Neither the staining capacity nor the white ash content of a cell seems to be related to the degree of pigmentation, however, as will be pointed out later.

In the outermost spinous cells (immediately adjacent to the granulosum) the cytoplasms look like splashed patches of deep bluish ash that is tinged here and there with very fine granules of red oxide of iron. The cell boundaries are not distinct, giving the impression that there is no peripheral layer of cytoplasm that is mineralized any differently than is the internal cytoplasm. In the same incinerated section of skin other cells, such as histiocytes and clear cells, show distinct cell membranes, thus precluding the probability that the membrane minerals were disturbed artificially. In every one of these outermost spinous cells the nucleus is surrounded by a cytoplasmic shell of white ash (fig. 1 *A*). This perinuclear mantle of white ash varies in thickness from about 2 to 4 microns and occupies approximately a fifth of the cytosome. This cloak of calcium and magnesium is wholly extranuclear, as can be determined easily by observing sections of the same cell cut at different levels; in some of these sections the perinuclear mantle of white ash apparently obliterates the nucleus, which in stained sections may be seen to be located at another level, while another section of the same cell shows a distinct nuclear area that is ashless. The nucleoplasm of these cells leaves very little ash as a rule with the exception of the thin film of grayish white granules in the nucleolar bodies and a few fine strands of white granules extending from them into the surrounding nuclear area. The nuclear membrane seems to be composed of granules of white ash with an occasional red granule of iron. The intranuclear area that is free of any white ash of calcium and magnesium exhibits no bluish ash that would presume the presence of sodium or potassium. Some of the intranuclear and extranuclear (perinuclear cytoplasmic mantle) ash of these outer spinous cells shows doubly refractive particles that are indicative of the presence of silicon probably in the form of silicocalcareous compounds. It is significant that the white ash in the corneum of the same sections exhibits no evidence of silicon. The intercellular fibrils of these outer spinous cells are not

heavily mineralized and frequently are not discernible by their ash residue. The intercellular spaces are filled with bluish ash that is free of any other ash and is distinct from the intracellular blue ash by its marked homogeneity. The intercellular ash is a clearer blue than is the intracellular ash, which appears grayish blue. The distinctness of this extracellular ash from the intracellular ash furnishes excellent evidence that the distribution of minerals has not been disturbed by condensation of water on cold sections of tissue previous to incineration, since one would expect to find the ash distributed evenly over intercellular and intracellular areas. How much of this intercellular ash is due to the presence of procaine hydrochloride that was injected at the time of obtaining the specimen for biopsy is questionable. However, aqueous solutions of this drug leave no ash when incinerated in droplet form on a slide, and sections of rat skin obtained with and without injections of procaine hydrochloride show no appreciable differences in ash within a reasonable length of time after injection. Specimens of skin of the same age taken with the patient under general anesthesia with no local injection of procaine hydrochloride appear no different from those taken after injection of the drug.

In the deeper spinous cells nearest the basal cell layer of infant epidermis, the cytoplasm and the nucleus are generally packed with dense masses of white ash of calcium and magnesium. The white ash of the cytoplasm may be distributed in clumps of granules or may be evenly distributed throughout, but there is invariably a thick perinuclear mantle of white ash (fig. 1 *A*). These cells contain considerable quantities of iron, particularly in the perinuclear mantle. In some cells small "holes" that are ashless may be found in the cytoplasm; these appear to be the spaces occupied by vacuoles in the living cells. Only a few of the intercellular fibrils leave any ash in infant skin. It is important to note here that the midregion of the intercellular fibrils is not thickened as in adult skin and the whole of each fibril is less intensely stained.

The nuclei of these deeper spinous cells in contrast to those of the superficially located cells are heavily mineralized. The nucleus is often nearly filled with white ash that is much whiter than the cytoplasmic ash. There is probably less blue ash of sodium and potassium in the nucleus so that the white ash is not tinged blue, as in the case of cytoplasmic white ash. Also, the granules of white ash are more closely packed together. The nuclear membrane is usually clearly outlined by a layer of white and yellowish granules. It is difficult to determine whether these granules are actually in the membrane or outside it. The ash of the nucleoli is usually indistinguishable except in nuclei having little white ash, in which the nucleolar ash is a bluish white.

Scattered throughout the deeper spinous cell layer at random are many isolated cells that leave no white ash of calcium and magnesium except a dense deposit of red iron oxide and white ash together in the nucleolus and a thin film of white and red ash granules in the nuclear membrane. The cytoplasms of such cells leave a bluish gray ash and stand out conspicuously among the heavily mineralized cells with white ash adjoining them (fig. 1 *A*). In the stained preparations of adjacent sections these isolated cells correspond to lightly stained cells that appear to be in an early stage of mitosis.

The basal cells of infant epidermis vary in the kind and amount of ash residue they leave after incineration. Beneath areas of very heavily mineralized spinous cells, the basal cells are also heavily mineralized; and beneath areas of low mineralization, the basal cells are also poorly mineralized. In areas of marked mineralization where the overlying spinous cells are full of white ash of calcium and magnesium, the basal cells generally contain a large bulk of white ash at the distal border of the cytoplasm and always around the nuclear membrane. Such ash is not associated with melanin pigmentation, as one might suspect, for melanin leaves no ash whatever. Indeed, in infant skin there is very little pigment visible. Most of the cytoplasm, however, exhibits a blue ash that is tinged grayish by the presence of widely separated granules of white ash (fig. 1 *B*). The nucleus is in every cell enclosed in a mantle of calcium and magnesium. The nuclear membrane leaves a film of ash beads consisting mostly of red iron oxide. The chromatin and nucleolus leave a dense white ash.

Scattered along the basal layer there may be found many clear cells whose cyptoplasm is almost free of white ash of calcium and magnesium. These clear cells leave usually a deep blue ash and sometimes no ash at all in the cyptoplasm, often appearing as a black space under dark field illumination among heavily mineralized cells. Their nuclei, however, leave considerable white ash in the nucleolar region, and there may be found many granules of iron oxide both in the perinuclear region and within the nuclear sap. The nucleus is therefore clearly outlined. It is important to state here that the nuclei of such cells are distinctly crescentic when seen in stained histologic preparations, owing usually to the presence of cytoplasmic vacuoles that invaginate a portion of the nuclear membrane. In the ashed section there is no evidence of this invagination of the nuclear membrane, probably because the ash of the overlying lips of the "crater" falls on incineration in such a way as to fill up the gap. This may account for the presence of a larger bulk of ash on one side of the nucleus in many instances. The cytoplasm of these clear cells protrudes into the dermis, where their blue ash may be readily distinguished by its clearness from the blue ash of the inter-

stices of papillary connective tissue. Judging by the ash residue, there are in young baby skin only two kinds of basal layer cells, namely, those few rounded clear cells containing large amounts of nuclear iron with but little white ash and those more numerous cylindric cells containing much white ash of calcium and magnesium in both the nucleus and the cytoplasm.

The dermis of young baby skin is heavily mineralized and shows much white ash of calcium and magnesium on incineration. This ash is deposited for the most part in connective tissue cells and in the collagenic fibers. In the dermal papillae there are many large fibroblasts that are loaded with great masses of white ash of calcium and magnesium. The walls of blood vessels contain much of it. Most of this white ash is doubly refractive, indicating the presence of silicon. The interstices of the connective tissues are filled with a grayish blue ash of the basal cells. In other places along the basal layer it is seen to be quite distinct from the basal cell ash.

Skins of Young Persons.—The epidermis evidently passes through a gradual change from infancy to maturity that is punctuated in early childhood by a fluctuating series of marked alterations which slowly become abated after 10 years of age to an evenly uniform continuous change that persists until old age. This seems clearly to be the case because so many young skins vary in their ash content from one extreme to another. The skin of a child 5 years of age may or may not contain mostly blue ash in the stratum germinativum. In a child 10 years of age the stratum germinativum is always packed with bluish white ash, and at the age of 15 it is heavily mineralized with a fat white ash. On the other hand, adult skins do not exhibit such extremes of hypermineralization and hypomineralization at different ages. At the age of 20 years the skin is heavily mineralized, and it continues thus, slowly increasing, until old age. The investigator cannot rely on the skin of very young subjects to maintain a constant mineral content, for it is only after the age of 10 years or more that the mineralization of the skin becomes a relatively static process.

The corneum of a young child's skin is always heavily mineralized with white ash of calcium and magnesium (fig. 2 *A*). This is in direct contrast to the mineralization of infant corneum, in which little white ash is found. Much of the ash in the corneum is combined with silicon, which is apparently increased in amount as the skin grows older. Other than the silicon content of the corneum, there are no visible variations in the ash of this layer in persons from 5 to 20 years of age. In the stratum granulosum of all young skin above infancy there are also dense deposits of white ash of calcium and magnesium in both the cytoplasm and the nucleus. The nucleus contains iron, and the large

incinerated nucleoli leave dense patches of white ash, much of which is silicon. The remainder of the nucleoplasm leaves a grayish white ash that is not doubly refractive. The whole nucleoplasm was apparently hypermineralized. The ash of the nuclear membrane is usually obliterated by the cytoplasmic ash. The white ash of the cytoplasm represents for the most part large closely packed keratohyalin granules.

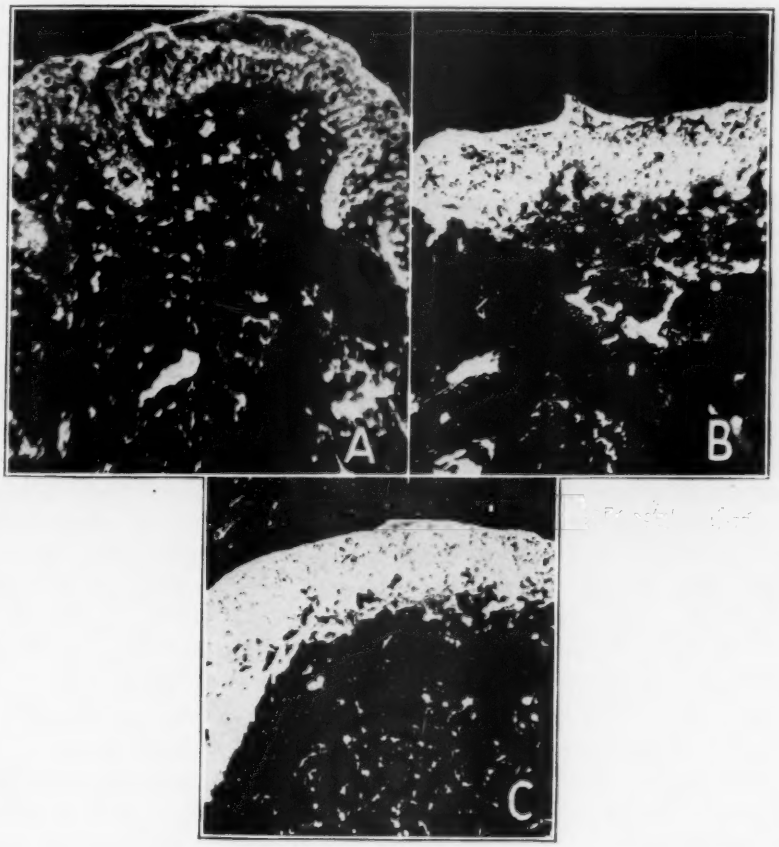

Fig. 2.—Normal skin (× 900) of (*A*) a 5 year old child, (*B*) a 20 year old person and (*C*) a 30 year old person.

The ash of the spinous cell layer varies from one specimen to another of the same age and from one age to another. After the age of 10 years, however, the ash content of this layer closely resembles that of adult skin. In a specimen from a child 6 years of age the spinous layer contained much white ash of calcium and magnesium, while in another specimen taken from the same region of a different person of the same age there was little white ash in the spinous layer of cells except in

the nucleoli and intercellular fibrils. In both instances the corneum and granulosum layers not only exhibited much white ash but were heavily keratinized. In both of two other specimens of skin from two different children 7 years of age, the whole spinous layer of cells was almost free of white ash of calcium and magnesium, except for thin films of perinuclear white ash and nucleolar ash. In all of our specimens from persons past 10 years of age, however, the whole skin was heavily mineralized with white ash. There are always clear cells present in the spinous layer whose nuclei contain much red oxide of iron and whose cytoplasm contains little white ash.

It is difficult to account for the presence of a great bulk of white ash of calcium and magnesium in the corneum, while almost none of it exists in the spinous cells. The nucleoli and intercellular fibrils are always discernible by their white ash residues regardless of the amount of white ash elsewhere in the section.

The basal cells never seem to vary much in their white ash content from infancy to old age. The amount of white ash in the peripherally located cells does not seem to be related to the amount in the basal cells, although in infancy there is a relationship. The basal cells show a considerable amount of white ash in the perinuclear and distal cytoplasm. Their nuclei are not heavily mineralized, and their nuclear membranes leave an ash consisting of white particles of calcium and magnesium and red granules of iron oxide. At all ages one may find many isolated clear cells containing blue ash in the cytoplasm and much iron in the nucleus scattered at random along the basal layer among the ordinary basal cells. These clear cells have already been described under infant skin.

The dermis does not vary much in its ash content throughout life. It contains a relatively static amount of white ash located for the most part in connective tissue elements, such as fibroblasts, and in some of the collagenic fibers. Most of the collagenic fibers appear blue, however. Much of the white ash is doubly refractive, which indicates the presence of silicon. There is a noticeable increase in dermal silicon in the skin of 20 year old persons as compared with that of infants.

Adult Skins.—The incinerated epidermis of adult skin (persons 20 to 50 years old) is generally heavily mineralized with white ash of calcium and magnesium. The corneum leaves a dense deposit of white ash, much of which is doubly refractive. There is little iron to be found in the corneum. Such iron is inorganic storage or excretory iron which can be readily detected with prussian blue. Often the corneum is not uniformly mineralized with calcium and magnesium, for bluish layers containing no white ash may be found. These bluish streaks are usually located above a layer of granular cells that leave bluish ash also (fig. 2*B*).

The granular cells are usually packed with large granules of white ash. These granules undoubtedly represent the mineral content of the keratohyalin granules, since they correspond in position to stained granules. The nucleoli also leave heavy deposits of white ash of calcium and magnesium with much silicon. There are large numbers of iron granules in the keratohyalin granules and many in the nuclei.

The spinous cells of adult skin are heavily mineralized, and there is always a thick perinuclear mantle of white ash of calcium and magnesium in each cell. Most of the cells contain a white ash of calcium and magnesium in their peripheral cytoplasms. The nuclei of these spinous cells contain much white ash that is sometimes patterned similarly to chromatin material. The nuclei contain a few scattered granules of iron oxide scattered throughout its white ash, and their membranes contain iron. Their nucleoli leave white ash heavily laden with silicon and some iron. The intercellular canals are filled with bluish ash when they are wide enough to be visible. Scattered about in the spinous layer there are a variable number of clear cells whose nuclei contain larger amounts of iron than do other ordinary spinous cells (figs. 2 *C* and 3).

The basal cells of adult epidermis leave mostly bluish ash with a thick perinuclear mantle of white ash. In some cells considerable white ash may be found in the distal cytoplasm. Pigment granules are not discernible by their ash, for they leave none that is apparent. However, it is usually in nonpigmented cells that calcium and magnesium are found in the distal peripheral cytoplasm. (The pigment granules when they are present are usually found in the stained sections at the proximal end of the cytoplasm toward the blood supply.) The clear cells in the basal layer are easily discernible by their lack of white ash and the presence of much intranuclear iron.

The dermis ash of adult skin is much like that of younger skin. The white ash is located in fibroblasts and on other connective tissue elements. Most of the white ash is doubly refractive, indicating the presence of silicon. The interstices of the connective tissue are more often free of any ash than full of it. Evidently the ashless spaces in the dermis represent ashless collagenic fibers. Other spaces are filled with blue ash but do not correspond in position to collagenic fibers in the stained preparations. There are no places where the white ash of calcium and magnesium is plastered along the under surface of the basal epidermal layer, although there are collagenic fibers placed longitudinally parallel to this surface. Such collagenic fibers apparently leave no white ash. The blood vessels have no white ash collars, but there are a few areas where some connective tissue cells that contain much white ash surround the blood vessels as a mild perivascular infiltration.

Senile Changes.—The primary change in old age appears to be a shift of the white ash of calcium and magnesium from the deeper portion of the epidermis to the corneum and dermis. Most of the cells

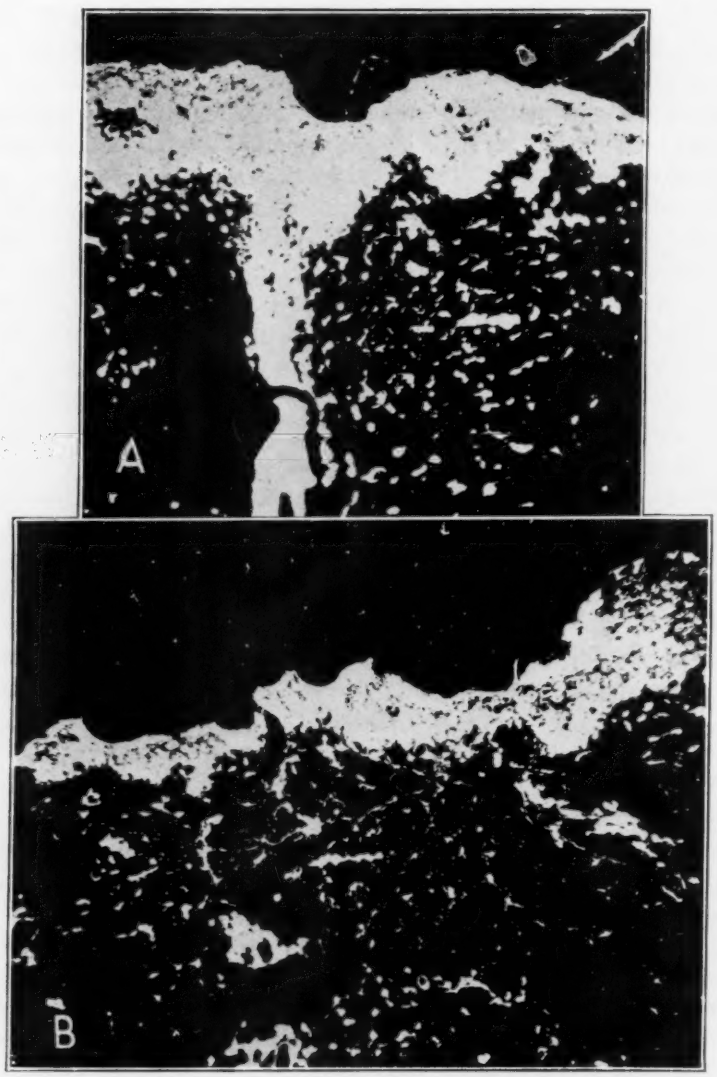

Fig. 3.—Normal skin (× 695) of persons (*A*) 40 years old and (*B*) 50 years old.

of the spinous and basal layers leave a blue ash, while the corneum and dermis are packed with white ash. Within the nuclei of many of the spinous cells there may be found large patches of red granules of

ash that are not iron but rather carbon (as determined by their blackness under transmitted light). This indicates some chemical difference in these nuclei that may account for their incomplete incineration of carbon compounds at the same rate and heat as nuclei of normal cells incinerate these compounds completely. There is less birefringent white ash in the dermis of old skin than in that of young skin.

Résumé of Mineralization of Normal Skin.—The ash content fluctuates between hypermineralization and hypomineralization in young skin until about the age of 10 years, when a definite change toward hypermineralization begins and proceeds slowly unbroken until old age. In the skin of infants under 1 year old, the stratum corneum, stratum granulosum and superficial spinous layer leave a bluish ash indicative of the presence of sodium and potassium, while the deeper spinous, basal and dermal layers contain much white ash of calcium and magnesium. In persons from 10 to 50 years of age all layers of the skin are heavily mineralized with white ash except the basal layer, which leaves mostly bluish ash. The basal cells, as well as the spinous cells, in the skin of persons between the ages of 10 and 50 years all possess thick perinuclear mantles of calcium and magnesium, except the "clear cells," whose ash is blue and whose nuclei contain large amounts of iron. In children between infancy and 10 years of age it is only the stratum corneum and stratum granulosum that are constant in their heavy deposits of white ash. The other layers may or may not be heavily mineralized. At all ages there are single clear cells more or less ashless scattered about in the spinous and basal layers. The nuclei of these clear cells contain an unusual amount of iron. Most of the collagenic fibers in skin at all ages are free of white ash of calcium and magnesium but leave considerable amounts of blue ash indicative of sodium and potassium.

ACTIVE NEURODERMATITIS LESIONS

Epidermis.—The corneum in every case of active lesions, regardless of the age of the patient, is heavily mineralized with white ash of calcium and magnesium (fig. 4*A*). Even in our one specimen of skin from a 15 month old patient with neurodermatitis the corneum left a dense deposit of white ash, whereas in a specimen of normal skin of the same age the corneum left a blue ash for the most part, with scarcely any white ash. The corneum of young neurodermatitis skin is heavily keratinized, as revealed by stained preparations, while the corneum of normal baby skin of the same age is not heavily keratinized. There seems to be some relation between the deposition of keratin and the degree of mineralization with white ash. Corneum that is richly keratinized leaves much white ash, while poorly keratinized corneum

leaves little white ash. The corneum of active lesions of all ages contains large amounts of silicon, the amount of which varies from one case to another and the source of which is probably extraneous. It is to be noted that the keratohyalin granules of the stratum granulosum in all active lesions are heavily mineralized with both white ash of calcium and magnesium and red ash of iron, except in those areas where parakeratosis has taken place immediately above the granular cells which leave only blue ash (fig. 4 *B*). Even in baby skin which normally shows little white ash in the keratohyalin granules, these granules in neurodermatitis lesions are heavily mineralized with it. Here again, it is only those granules that stain deeply with ponceau xylidine (probably heavily keratinized) which leave white ash residue on incineration. The granules and corneum of normal baby skin therefore resemble parakeratotic epidermis of neurodermatitis skin both in staining qualities and in mineralization.

The spinous cells in active lesions of neurodermatitis are large and contain very little white ash except for a thin ring around the nuclear membrane (fig. 5 *A*). The ash for the most part is bluish under dark field illumination. Granules of white ash are rarely ever seen in any of the spinous cells in the most active lesions in which the suprapapillary epidermis is frayed and edematous. However, as one proceeds from such an active area to cells in the less active area surrounding the active lesion, most of the spinous cells possess a bluish gray ash in their cytoplasm, which consists mostly of clear bluish ash. It is difficult to distinguish the ash of most of the spinous cells of such quiescent areas from that of spinous cells of active areas, although quiescent areas contain many isolated cells scattered throughout the spinous layer that seem to have retained their white ash in normal amounts. It is only in active areas that all the spinous cells have lost their calcium and magnesium constituents. In every case of active lesion, regardless of age, the spinous cells have lost most of their white ash of calcium and magnesium. It is safe to say that the only calcium and magnesium left in these cells is that around the nuclear membranes and that contained within the nuclei. This is true of all spinous cells above the basal layer in active lesions. There is in some cells a peripheral border of bluish white granular ash that might indicate the presence of a cell membrane. But in most cells there is no ash residue at the peripheral border of the cytoplasm that is any different in its physical properties than the ash of the internal cytoplasm. It seems unusual that there should be no border of calcium.

The intercellular fibrils in most areas where they are thickened in active lesions leave dense deposits of white ash in the vicinity of their "midbulbs," which lie between cells. The remainder of each fibril rarely leaves a distinguishable ash.

The nuclei of spinous cells in active lesions contain white ash in their polynucleolar bodies and sometimes in the nuclear sap. It is significant that this white ash does not contain silicon, since so much

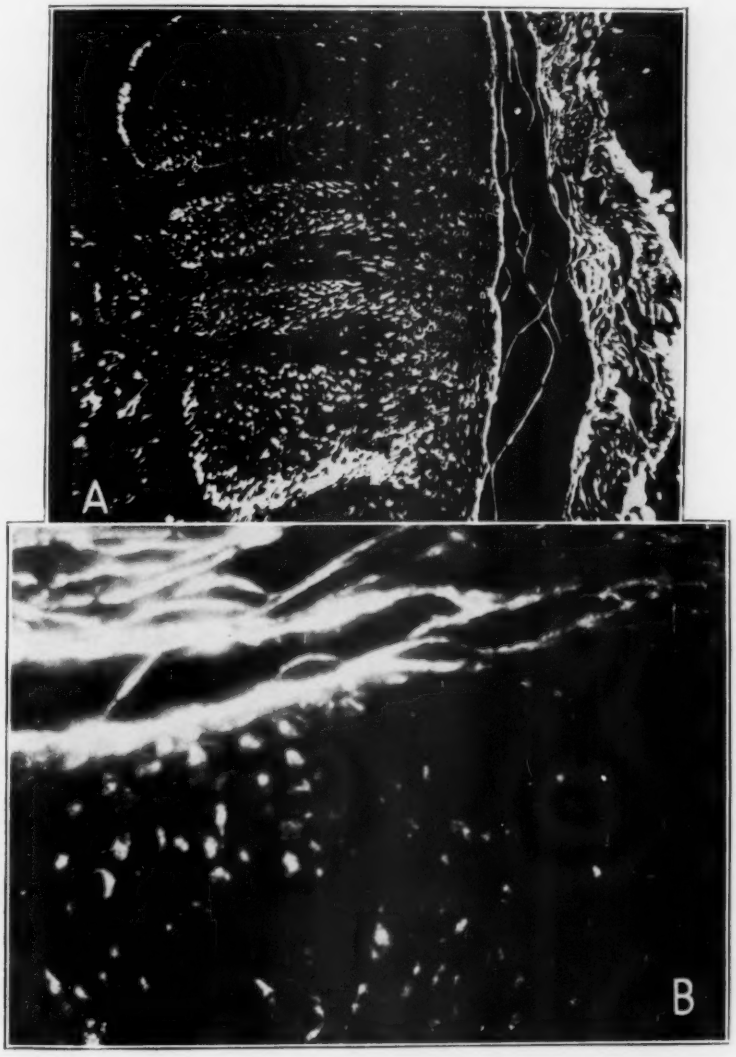

Fig. 4.—Active lesions of neurodermatitis. *A*, note heavy mineralization of corneum with white ash of calcium and magnesium, lack of white ash in spinous layer and little in basal cell layer (× 650). *B*, portion of epidermis at junction of corneum and granular cells (× 795). On left side of picture note hypermineralization of both granular cells (keratohyalin granules) and corneum, while on right side is shown lack of white ash both in granular cells and in corneum.

silicon appears in the corneous cells. Most of the extranucleolar ash of the nuclei of the peripheral spinous cells in active lesions consists

of iron. In some areas all of the spinous cell nuclei contain huge amounts of iron that seems to have been contained in the nuclear sap, since there is no arrangement of its particles that would indicate a

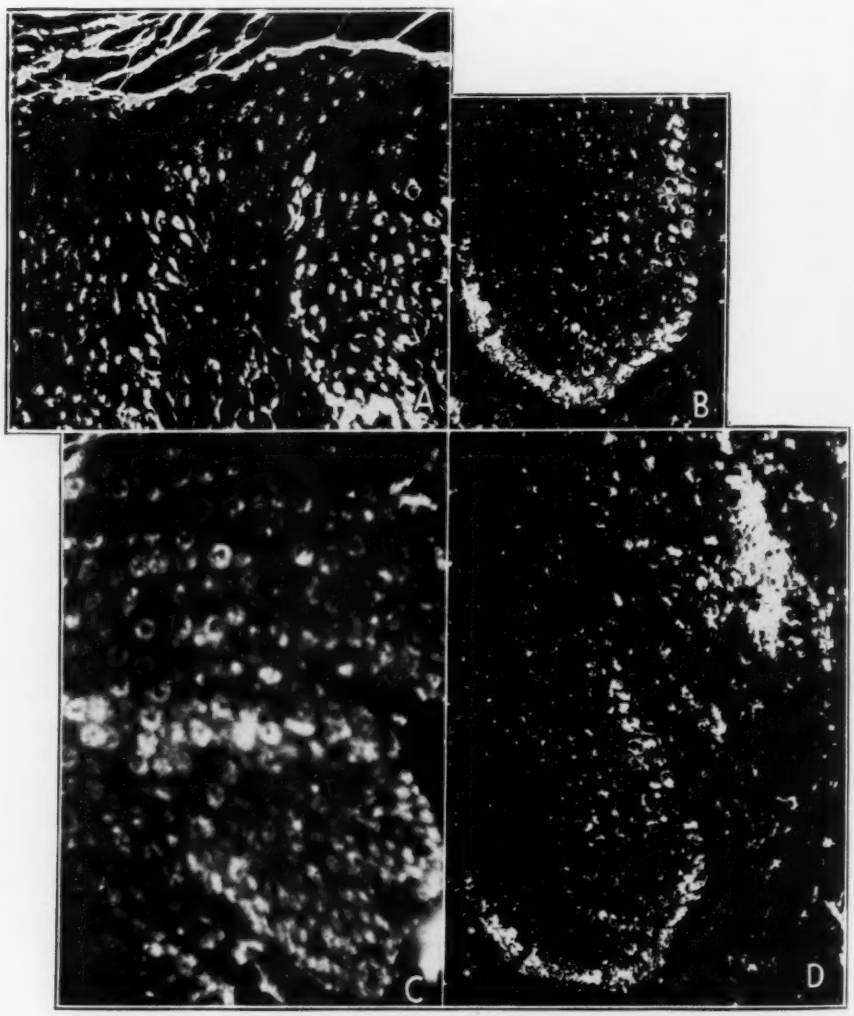

Fig. 5.—Active lesions of neurodermatitis, showing (*A*) ash of spinous cells and disintegrating basal cells (× 565); (*B*) ash in proximal ends of cytoplasms of basal cells (× 565); (*C*) ash-free nucleoli and ash-rich nucleoli, which contain no silicon, as do normal nucleoli (× 720), and (*D*) ash in proximal ends of cytoplasms of basal cells (same as fig. 5 *B*).

chromatin network and the red ash is not contained in compact bulks such as appear in the white ash of the nucleoli.

The nature of the excess iron in active lesions seemed important enough to warrant comparison of the iron in neurodermatitis skin with that in normal skin. By application of histochemical tests for iron, it is possible to distinguish between inorganic storage iron and biologically active organic compounds of iron. The ordinary prussian blue test for iron was compared with the well known Macallum test for organic compounds of iron. Prussian blue will ordinarily react only with inorganic iron. But by Macallum's method the tissue section is first extracted with acid alcohol to remove the inorganic iron and free the organic masked iron, and then the section is flooded with prussian blue. Macallum's test detects only organic masked iron, such as that found in cytochrome and nucleoprotein compounds of the nucleus.

In normal skin from normal persons nearly all the iron is organically bound masked iron detectable only by Macallum's test. Little of it is storage iron.

In unaffected skin and lesions of patients with neurodermatitis almost all of the iron is held in the inorganic state detectable by the ordinary prussian blue reaction. Scarcely any iron is seen in Macallum preparations of such skin. The intranuclear iron of the spinous cells of active lesions is almost entirely inorganic iron.

Healed neurodermatitis lesions contain large amounts of inorganic iron in the corneum, but the remainder of the skin contains organically bound masked iron with little inorganic iron.

The deeper spinous cell nuclei near the basal cells of active lesions contain iron as do the superficial nuclei but not in such large amounts. However, scattered at random throughout the deeper spinous layer there may be found many isolated cells whose nuclei contain as much iron as do the nuclei of the superficial spinous cells of active lesions. The membranes of these spinous cell nuclei in every case consist of thin films of fine red and white granules of iron, calcium and magnesium.

It is pertinent to observe here that not all of the nucleoli of a single spinous cell leave white ash of calcium and magnesium (fig. 5 *C*). The nucleoli which stain heavily with ponceau xylidine leave the most conspicuous deposits of white ash. Further, the nucleoli of the spinous cells nearest the basal layer frequently leave no ash. It is also important to note that the nuclei do not leave bluish ash. In areas where no ash of silicon or iron or calcium exists, the dark field area appears simply black (or entirely ashless). Hence, it would seem that the nucleus contains little or no potassium and sodium (and the blue ash has been shown to contain those two elements always).

The intercellular spaces in active lesions contain a clear bluish ash that is easily distinguishable from the slightly grayish blue ash of the spinous cells. The borders of the spinous cells can be delimited from the intercellular spaces, although no cell membrane residue can be

distinguished. There is no white ash in the intercellular spaces. It appears that these canals possess delimiting membranes that contain ash, for in areas where the swollen canals have protruded into the dermis [2] the walls of such channels leave a fine white ash of calcium and magnesium. It is possible that such films of ash may have originated from the dermal spaces and merely adhered to the surface of the intercellular space, but it still suggests that these spaces are structurally delimited. The observation of ash under oil immersion lenses is difficult.

In some cases of active lesions of neurodermatitis there are circumscribed patches of spinous cells whose nuclei may be surrounded by single vacuoles. In many instances there may be polar vacuoles, which we have designated as "distal polar" and "proximal polar" vacuoles.[2] These vacuoles are confined to the cytoplasm and merely invaginate the nuclear membranes. The proximal polar vacuoles leave a bluish ash residue, while the distal polar and the single circumnuclear vacuoles leave no ash at all.

We have pointed out elsewhere [2] that the outermost spinous cells in active lesions of neurodermatitis are colored intensely with a dye having affinity for collagen (aniline blue), while the deeper spinous cells of the same area may stain lightly with acid fuchsin. The ash residue of the outermost, bluish-colored spinous cells generally differs markedly from that of the deeper, reddish–stained cells. Although this difference is not entirely uniform in its appearance throughout all areas of a given lesion, it is always recognizable in spots surrounding an area where the epidermis is thinned overlying a highly edematous papilla (indicating that the epidermis is on the verge of breaking down completely in that particular region). The cytoplasmic ash of the outermost spinous cells consists of a clear blue ash, and the nuclei contain much iron oxide. On the other hand, the cytoplasmic ash of the deeper spinous cells in almost all instances appears as a distinctly grayish blue (indicating the presence of widely separated granules of white ash), and the nuclei contain less iron. It seems, then, that the spinous cells in active areas of a lesion undergo a change in staining capacity that is evidently concomitant with a change in the intracellular minerals. This change is not conspicuous in less active areas where there are no signs of thinning and breakdown of the epidermis. It is evidently a gradual change that quickly becomes exaggerated enough, in the late stages of the development of a lesion, to be readily observable. The nature of such changes will be discussed later.

The nuclei of the deeper spinous cells in an active area contain less iron oxide residue than do the outermost spinous cells. It appears that the nuclei of the outermost spinous cells absorb iron from the cytoplasmic supply and hold it tenaciously, while the deeper spinous cell nuclei have absorbed little of this element.

The ash of most of the basal cells in active lesions does not differ markedly from that of the basal cells in normal skin. They usually contain thick perinuclear mantles of white ash that is speckled with red granules of iron oxide, just as in normal basal cells.

However, in some areas which may be shown to be located in very active inflammatory areas of a lesion, most of the white ash of the basal cells is confined to the proximal ends of the cytoplasm (fig. 5 *B* and *D*), the distal surface of the nucleus being left essentially naked except for a thin layer of white ash with red granules. This is particularly true of basal cells surrounding an area of frayed basal cells overlying an edematous papilla where the epidermis is thin. Such a lack of white ash of calcium and magnesium in the distal cytoplasm would seem to suggest that these cells exhibit a polarity in respect to the absorption of minerals. It is difficult to determine whether the calcium and magnesium were drained out of the distal end of the basal cell and absorbed by the spinous cells that were deprived of these elements or whether the calcium and magnesium of the distal cytoplasm of the basal cell simply became changed somehow into more finely divided particles which failed to leave a white ash on incineration. The blue ash residue of the distal cytoplasm of such an apparently polarized cell shows a grayish cast, indicative of the presence of some white ash granules, which on examination with the oil immersion lens appear bluish gray intermingled with promiscuously located reddish yellow granules of iron oxide.

Scattered throughout the basal cell layer there are numerous isolated clear cells whose cytoplasmic areas frequently are ashless and less often filled with a bluish ash. Their nuclei contain considerably larger quantities of iron oxide than do their immediately adjacent basal cell neighbors. These clear cell nuclei possess also much white ash which exhibits little evidence of the presence of silicon. It is interesting that these nuclei rarely contain much discernible blue ash, even in those cases in which there is little intranuclear white ash, where the blue ash should be easily distinguishable.

Dermis.—The dermis in areas of active lesions of neurodermatitis leaves a large amount of white ash that is located for the most part in connective tissue cells, such as fibroblasts and large monocytes, and plastered on the surfaces of collagenic fibers. The collagenic fibers consist of a thick core of blue ash with a shell of white ash. Frequently one may see thick collagenic fibers that consist entirely of white ash, but on examination of such fibers in the next section it will be seen that they generally possess cores of blue ash. It is easily demonstrable both in normal and in neurodermatitis skin that the white ash content of collagenic fibers is superficially deposited. In some other cutaneous diseases, such as exfoliative dermatitis, as will be pointed out later,

the whole collagenic fiber is impregnated with calcium and magnesium and surface deposition is only rarely demonstrable. There is a great deal of silicon present in the white ash of the dermis but not enough to account for the huge amounts of this element found in the corneum of neurodermatitis skin.

The interstitial spaces between the collagenic fibers and other connective tissue elements are generally filled with a clear blue ash. However, immediately beneath the basal cell layer such interstitial blue ash appears grayish white. Often such grayish blue ash of the interstitial spaces can be conspicuously distinguished from the ashless cytoplasms of clear cells whose cytosomes protrude into the dermis.

The ash residue of the blood vascular system is interesting, particularly in regions where perivascular infiltration collars surround the capillaries. As has been pointed out before,[2] some investigators believe that the blood vascular system is the primary shock tisue in the development of a lesion. The mineral content of the wall of the blood vessel does not appear to differ from that of a vessel from normal skin. Even in areas of marked perivascular infiltrations, the walls of blood vessels contain normal-looking amounts of white ash. Such vessels are always surrounded by connective tissue cells (fibroblasts and monocytes) which leave much intracellularly located white ash on incineration. All of the connective tissue elements and the blood vessel as well seem to have been embedded in a groundwork of fine collagenic fibrils and fluid whose ash residue consists mostly of blue ash. This blue ash of the connective tissue spaces contains considerable carbon-containing compounds, for the blue extracellular ash is usually speckled with small particles of red ash that may be identified as carbon. Hence, it appears that the contents of the tissue spaces around these perivascular infiltrations do not incinerate as completely as do the intracellular components of the connective tissue cells. Such incomplete incineration of extracellular substance rarely occurs in the dermis of normal skin.

In active lesions that are highly edematous there are often as many connective tissue cells (monocytes, fibroblasts, etc.) scattered about the dermis immediately beneath the basal layer of the epidermis as there are around inflammatory blood vessels where perivascular infiltrations occur. Frequently the dermis of a swollen papilla contains numerous free cells which are not associated with blood vessels. Free dermal cells that are not associated with perivascular infiltrations are heavily loaded with white ash of calcium and magnesium, just as are the cells composing perivascular infiltration (fig. 6*A*). It is difficult to ascertain the relationship between such subepidermal cells and those of the perivascular infiltrations. However, in view of the fact that changes in the spinous cells most often occur before perivascular inflammation sets in, it is possible that the subepidermal connective tissue cells represent

cells that have migrated from the perivascular infiltration area after having absorbed calcium and magnesium from the blood stream to supply these elements to epidermal cells that are presumably becoming depleted of calcium and magnesium.

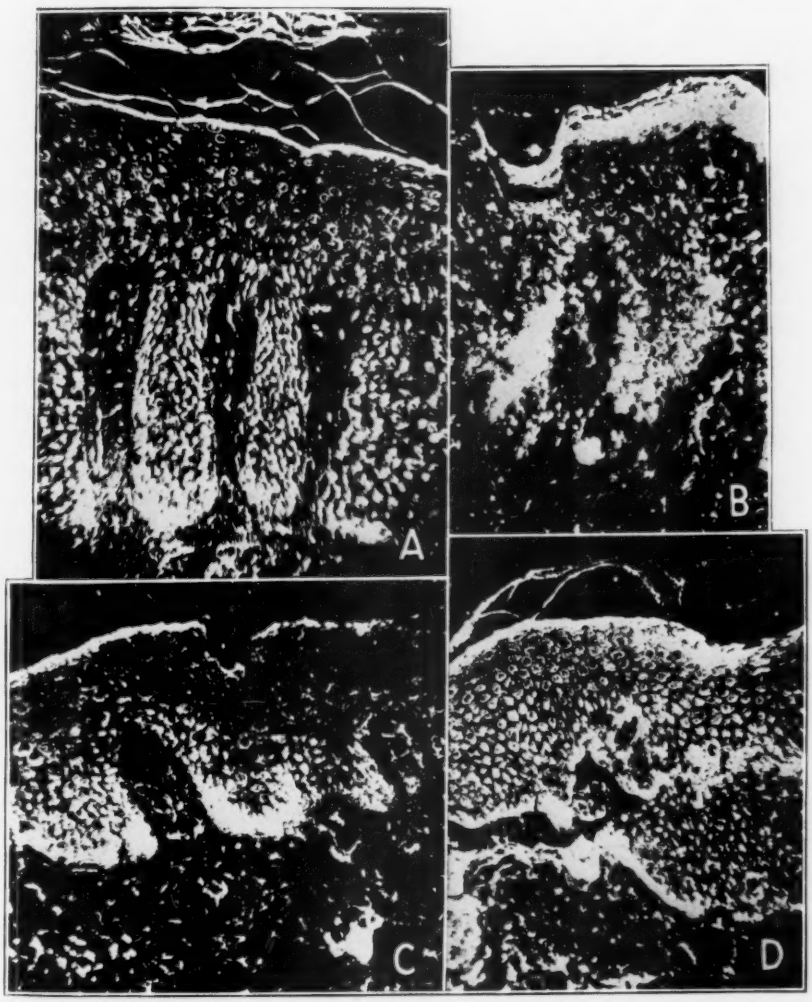

Fig. 6.—*A*, active lesion of neurodermatitis, showing ash of the dermis (× 600); note white ash in subepidermal cells. *B*, unaffected skin of patient aged 18 with neurodermatitis (× 600); note heavily mineralized corneum and granular cells; spinous cells lack white ash. *C*, unaffected skin of patient aged 22 with neurodermatitis (× 600); note that some spinous cells contain much white ash of calcium and magnesium, while other spinous cells contain very little ash. *D*, unaffected skin of patient aged 6 years with neurodermatitis (× 600); note same characteristics as in figure 6 *C*.

In the peripheral areas of the skin surrounding an active lesion in neurodermatitis there are fewer subepidermal cells and the perivascular infiltration collars are not as extensive or as thick. The perivascular infiltration cells of such peripheral (less active) areas of skin are not as heavily laden with white ash, although the spinous cells contain much less of this ash than do normal spinous cells. The subepidermal cells in these less active regions often leave much blue ash as well as white ash of calcium and magnesium. Thus, it may be seen that the perivascular infiltration cells probably do not absorb much calcium and magnesium and do not migrate to the epidermal juncture until long after the spinous cell layer has begun to lose its calcium and magnesium. Further, the development of perivascular infiltrations apparently lags far behind the rapid changes in the epidermis.[2] Hence, if significant mineral changes do occur at all in the walls of the blood vascular system, they probably occur secondarily (chronologically at least) to the mineral changes in the epidermis.

UNAFFECTED NEURODERMATITIS SKIN

Specimens of unaffected skin were obtained from the thoracic region of the midaxillary line of patients who were suffering from antecubital lesions of neurodermatitis. Lesions had never occurred in the region of the midaxillary line in these patients, and they rarely ever occur there.

Epidermis.—The corneum of unaffected neurodermatitis skin is heavily mineralized with white ash of calcium and magnesium (fig. 6 *B*). It has been noted previously [2] that this layer is remarkably thicker than that of normal skin. The keratohyalin granules of the granular layer leave distinct deposits of white ash.

Most of the spinous cells leave a bluish gray ash that is speckled with granules of white ash. However, many isolated cells and sometimes groups of cells are heavily laden with white ash (fig. 6 *C* and *D*). Such a bluish gray background of spinous cells with conspicuous white patches of single cells and groups of cells is characteristic of unaffected neurodermatitis skin. This appearance is easily recognizable and thus clearly distinguishes the ash residue of unaffected neurodermatitis skin from that of normal skin in which there is a white ash background of spinous cells with a few isolated clear cells whose ash is blue. Most of the spinous cells do not possess thick perinuclear mantles of white ash as do cells from normal skin. However, the isolated cells and groups of cells leave much white ash in the vicinity of the nucleus. In unaffected neurodermatitis skin even the spinous cells nearest the basal cell layer leave little white ash around the nucleus.

In unaffected neurodermatitis skin it appears, then, that the calcium and magnesium content of most of the spinous cells has been reduced,

while in some isolated single cells and groups of spinous cells the normal amounts of these elements have been maintained or actually augmented. It is difficult to determine whether spinous cells whose ash is bluish gray with little white ash have lost previously absorbed calcium and magnesium or have simply been disorganized to such an extent that they are unable to absorb biologically sufficient quantities of these minerals. In some areas of unaffected neurodermatitis skin, all the spinous cells are loaded with white ash of calcium and magnesium. However, in such areas where all the spinous cells are loaded with white ash, there are no clear cells scattered throughout the spinous layer as in normal skin. In normal skin such clear cells leave a distinct blue ash and are easily distinguishable from the remainder of the spinous cells. Since there are these few areas of spinous cells that are densely packed with white ash, it seems reasonable to suppose that all other spinous cells at one time or another contained much white ash of calcium and magnesium but that they lost most of these elements later. This probably constitutes a fluctuating process in unaffected skin; the spinous cells are all heavily mineralized with calcium and magnesium, and then they lose these elements. The white ash is very likely calcium for the most part, since the spectrogram of such unaffected neurodermatitis skin shows a large amount of calcium in most cases and always a low magnesium content.[1] However, it is not safe to conclude from spectrographic analysis that the white ash contained in the heavily mineralized spinous cells is mostly calcium, for the excess calcium recorded on the spectrogram may represent the calcium of some other part of the skin, while the magnesium content of other parts of the skin rather than that of the spinous layer may have been diminished. But since most of the spinous layer of unaffected neurodermatitis skin lacks white ash (and it is very probable that all of the magnesium would be represented by white ash), and since this ash is diminished in no other layer of the skin, one may say that a lack of magnesium in the spinous cells is in part at least responsible for the low magnesium recorded spectrographically.

The intercellular fibrils may be identified in incinerated unaffected neurodermatitis skin by their white ash. This is especially true over areas that have little pigment.

The basal cells of unaffected neurodermatitis skin leave a considerable white ash residue after incineration. Although in general the ash of this cellular layer resembles very closely that of basal cells from normal skin, in some places one may find a long row of basal cells whose ash is mostly blue. This is particularly true in areas that are nonpigmented. However, there is no evidence of any relationship between the deposition of white or blue ash and pigmentation, for many pigmented cells also leave a bluish gray ash. There are many clear cells in the basal layer

of unaffected skin. These cells are for the most part ashless, although their nuclei contain white ash.

Dermis.—The collagenic fibers of the dermis of unaffected neurodermatitis skin leave dense deposits of white ash (fig. 6 *B* and *C*). Evidently the whole of each fiber is infiltrated with calcium and magnesium. This is not true of collagenic fibers from normal skin. In the dermal papillae of unaffected neurodermatitis skin, however, the collagenic fibers leave a blue ash. Much of the white ash of the deeper dermis is doubly refractive, indicating the presence of silicon. The chromatophores of the dermis leave little white ash.

HEALED NEURODERMATITIS LESIONS

Six specimens of healed lesions were obtained from the region of the cubital fossa. Two of the patients were suffering from lesions elsewhere, while the other 4 had no detectable lesions elsewhere at the time specimens were taken for biopsy.

Epidermis.—The corneum of healed lesions of neurodermatitis skin is heavily mineralized with white ash and red granules of iron oxide (fig. 7) except in areas where extensive patches of parakeratosis exist. In most respects the ash of the corneum of healed lesions resembles closely that of active lesions. Likewise, the granular layer is similar, except that part lying beneath areas of parakeratosis. The keratohyalin granules leave a dense white ash of calcium and magnesium intermingled with red iron oxide beneath areas of the corneum that are heavily keratinized and heavily mineralized, while beneath areas of corneum that show every evidence of parakeratotic processes at the time the specimen is removed for biopsy the keratohyalin granules and indeed the whole cytoplasms of the granular cells leave bluish ash with little white ash and no iron.

The spinous cells in healed lesions are usually all conspicuously mineralized with large bulks of white ash of calcium and magnesium (fig. 7). One may often find the reverse picture of the patchwork pattern described for unaffected skin. In healed lesions most of the cells contain huge masses of white ash which often obscure the nuclear ash, with a few isolated single and groups of spinous cells containing little white ash. The spinous cells of healed lesions are even larger oftentimes than those of active lesions, yet they may contain more white ash than either cells from active lesions or cells from normal skin. By rough estimate under the microscope, it is safe to state that most of these spinous cells from healed lesions contain twice as much white ash as do spinous cells from normal skin. Evidently, the biologically essential amounts of the elements represented by this white ash of spinous cells of healed lesions are at least twice as great as those of normal spinous cells. These spinous cells in healed lesions have

increased not only in size but also in biologically essential requirements of minerals. Hence, it is altogether logical to assume that spinous cells of active lesions (in which it is possible that amounts of calcium and

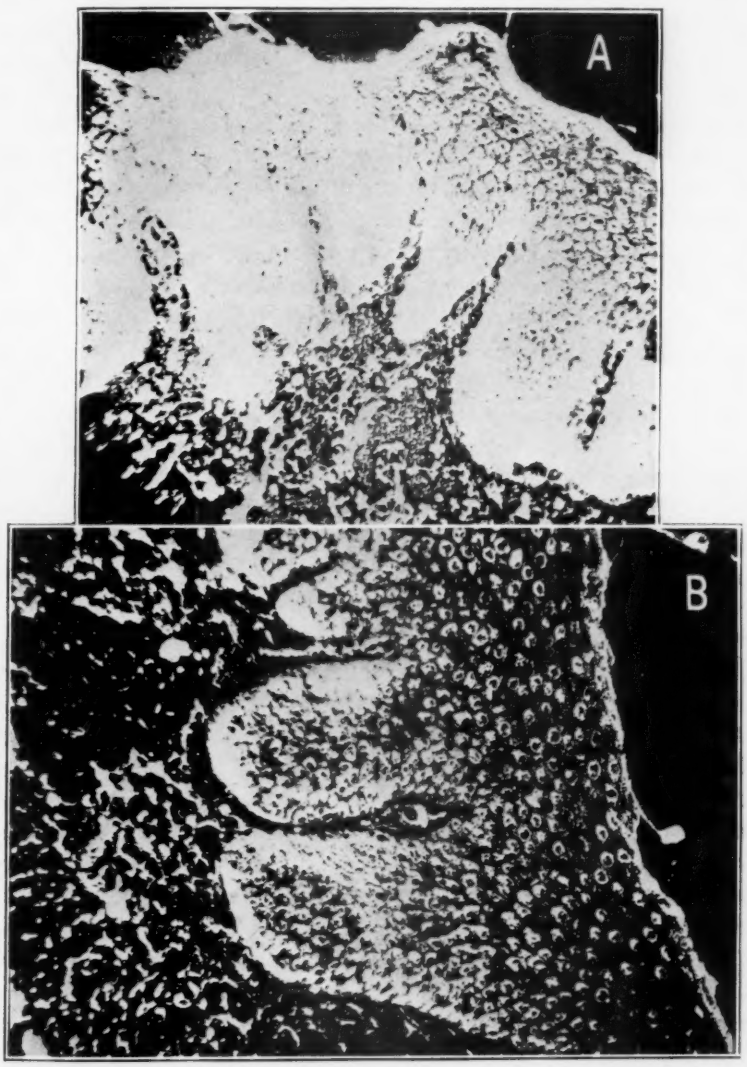

Fig. 7.—*A*, healed lesion of neurodermatitis of patient aged 18 (× 640); lesion has been healed for two months; note heavy deposition of white ash, which consists of calcium, magnesium and silicon. There is also much iron, which cannot be distinguished here. *B*, early healed lesion of patient aged 18 with neurodermatitis (× 640); note heavy deposition of white ash in nucleoli which contain calcium and silicon.

magnesium equivalent to those in normal cells are present but merely scattered over a greater cytoplasmic area) lack sufficient quantities of

calcium and magnesium, since healing epidermal lesions obviously require more than twice the amounts of normal cells of these elements for repair of damaged epidermis.

The intercellular spaces are for the most part obliterated in healed lesions. However, most of the intercellular fibrils are clearly definable by their white ash residues, especially under areas where the corneum is heavily keratinized.

The nuclei of the spinous cells leave much white ash and much red oxide of iron. This is true of all spinous cells. The nuclear contents of spinous cells in healed lesions contain iron deposits that are detectable with Macallum's test for organic iron but not with ordinary prussian blue without acid alcohol extraction. This shows that most of the iron must be organic active iron contained as cytochrome or some other iron compound. The intranuclear white ash of spinous cells in healed lesions is usually doubly refractive. The intranuclear white ash of active lesions, on the other hand, shows little doubly refractive ash, indicating a lack of silicon.

It is clear, then, that spinous cells of active lesions in order to promote healing processes have evidently been able to absorb more calcium and magnesium and that the iron has been bound into active organic compounds that are usable in metabolism, in contrast to the inorganic iron in developing active lesions. In addition to these changes during healing, the nucleus has regained not only more calcium and magnesium but also more silicon.

The ash of the basal cells of healed lesions resembles very closely that of basal cells in normal skin. Almost every basal cell shows a thick perinuclear mantle of white ash in the distal cytoplasm, like that in the proximal end of the cell. It appears that the basal cells of healed lesions contain more white ash than do the basal cells either of lesions in any other stage of the disease or of normal skin. This increase in bulk of white ash is probably due to the increased size of the cytosome and nucleus of each basal cell, just as there is an increase in white ash accompanying increase in size of spinous cells in healed lesions. The basal cells contain some iron. Some of the basal cells in healed lesions exhibit varying degrees of pigmentation, but most of them have no pigment at all. There is no evidence, however, that the pigmented granules leave any white ash. Nonetheless, spinous cells and corneum overlying areas of heavily pigmented basal cells usually contain less white ash of calcium and magnesium than do corneum and spinous cells overlying nonpigmented basal cells.

The ash of clear cells in healed lesions is not so clearly distinguishable from that of other cells as it is in other specimens, such as those of active lesions. In healed lesions the ash of the clear cells consists mostly of white ash of calcium and magnesium, whereas in normal skin and

active lesions it consists of blue ash, which is indicative of the presence of much potassium and sodium. The nuclei of clear cells in healed lesions do not contain as much iron as do those in active lesions.

Dermis.—The dermis of healed lesions is thickly bound with collagenic fibers whose ash residue consists largely of white ash of silicon and magnesium and calcium. Even in the papillae, the ash contains much doubly refractive white ash of silicocalcareous compounds. It appears that the healing process involves a mobilization of silicocalcareous material and magnesium to the dermis. Such bulks of white ash are present in the dermis not only of old healed lesions but also of recently healed ones.

There are many chromatophores in the dermis whose pigmented granules are irregularly shaped and filled with a flat white ash of calcium and magnesium and with particles of iron oxide. Such pigmented substance is probably not all melanin, since melanin does not leave any residue of iron and leaves little white ash.

The perivascular infiltration in healed lesions resembles very closely that of active lesions, and the infiltrating cells contain much white ash. In the dermal papillae, however, there are many more fibroblasts and monocytes in healed lesions than there are in active lesions. Such freely moving cells in healed lesions are always filled with white ash of calcium and magnesium, and their nuclei contain silicon.

OTHER DISEASES OF THE SKIN

A total of 55 specimens from patients with twelve different cutaneous diseases other than neurodermatitis were studied by microincineration. Only five of these diseases resemble chronic disseminated neurodermatitis clinically or histologically,[2] namely, lichen simplex chronicus, exfoliative dermatitis, infantile dermatitis, chronic contact dermatitis and psoriasis. The essential histologic features of these diseases are to be found in our previous paper on the histology of neurodermatitis.[2] None of these twelve diseases is associated with a lack of magnesium in the skin,[1] and with some of them there is an excess of this element.

Localized Neurodermatitis.—Localized neurodermatitis, or lichen simplex chronicus, is generally acknowledged to be an essentially different disease from generalized, or disseminated, neurodermatitis. From our 6 specimens of this disease we were unable to distinguish it unequivocally as a histologic entity distinct from chronic disseminated neurodermatitis.[2] However, we described certain marked differences between these two types of neurodermatitis. Briefly, these differences were: (1) a double row of basal cells in localized neurodermatitis, in contrast to a single row in disseminated neurodermatitis; (2) the presence in localized neurodermatitis of large vacuoles in the corneum whose contents stained with a dye having affinity for collagen (aniline

blue) in contrast to the red stain adsorbed by the surrounding keratin (such vacuoles have not been seen in any cases of disseminated neurodermatitis), and (3) the disintegrated basal cells that lie beneath intact spinous cells (whereas in disseminated neurodermatitis the basal cells always remain intact until the spinous cells have disintegrated).

The ash residue of incinerated sections of skin of patients with localized neurodermatitis is markedly different from that of skin of patients with chronic disseminated neurodermatitis (figs. 5 *A* and 8 *A*). In active lesions of localized neurodermatitis most of the spinous cells of the epidermis are filled with white ash of calcium and magnesium, in contrast to the lack of these elements in spinous cells in active lesions of chronic disseminated neurodermatitis. The basal cells of localized neurodermatitis are also filled with this white ash even in spots where the basal layer is disintegrating. The spinous cells overlying the disintegrating basal cells contain much white ash. There is not a single area in active lesions where the spinous cells do not possess at least a thick perinuclear mantle of white ash of calcium and magnesium. The corneum is heavily mineralized with white ash except the substance within the vacuoles previously described, which leaves a bluish ash. These vacuoles in the corneum of localized neurodermatitis lesions may be easily distinguished by their huge, clearly outlined patches of blue ash within corneum that is densely packed with white ash.

Just where the primary reaction in localized neurodermatitis is to be found is difficult to tell from our specimens, which are all from active lesions. However, the most conspicuous change as compared with normal skin from normal persons seems to be a mobilization of calcium and magnesium to the epidermis rather than a loss of these elements, as in chronic disseminated neurodermatitis.

Exfoliative Dermatitis.—Histologically, skin of patients with exfoliative dermatitis differs from that of patients with chronic disseminated neurodermatitis in that its corneum is poorly keratinized and its basal cells poorly stained with acid fuchsin, whereas in active lesions of chronic disseminated neurodermatitis the corneum is richly keratinized and the basal cells heavily stained with acid fuchsin.[2]

In ashed sections of active lesions of exfoliative dermatitis, the corneum is not heavily mineralized with white ash of calcium and magnesium (fig. 8 *C*). The basal cells have less white ash than normal basal cells, while the spinous cells are loaded with masses of white ash that obliterates cell boundaries. Most of the nuclei contain little white ash, however. The dermis contains much flat white ash that is comparatively free from silicon.

Infantile Dermatitis.—Study of the ashed sections of this skin is interesting because the disease is believed to be the forerunner of neurodermatitis. Our single specimen shows that the whole epidermis

is loaded with white ash of calcium and magnesium (fig. 8 *B*). The nuclei contain much silicon. The keratohyalin granules leave much white ash, which is in contrast to the ashless keratohyalin granules of

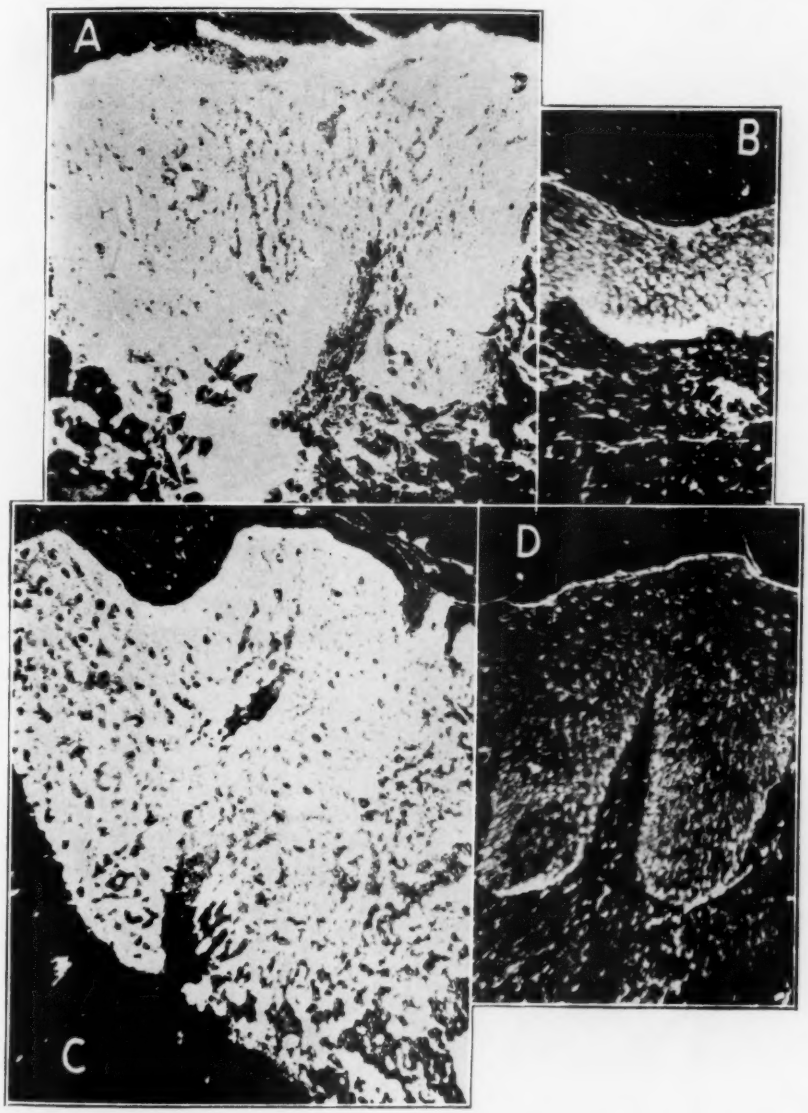

Fig. 8.—Lesions of dermatitis (× 710). *A*, active lesion of localized neurodermatitis (lichen simplex chronicus) of patient aged 20; note similarity between this active lesion and a healed lesion of disseminated neurodermatitis (fig. 7 *A*). *B*, active lesion of infantile dermatitis. *C*, active lesion of exfoliative dermatitis. *D*, chronic lesion of contact dermatitis.

normal baby skin. It is significant that the corneum of this infantile dermatitis skin contains much white ash, whereas the corneum of normal baby skin leaves a bluish ash. The corneum of active lesions of neurodermatitis in infant skin also leaves much white ash.

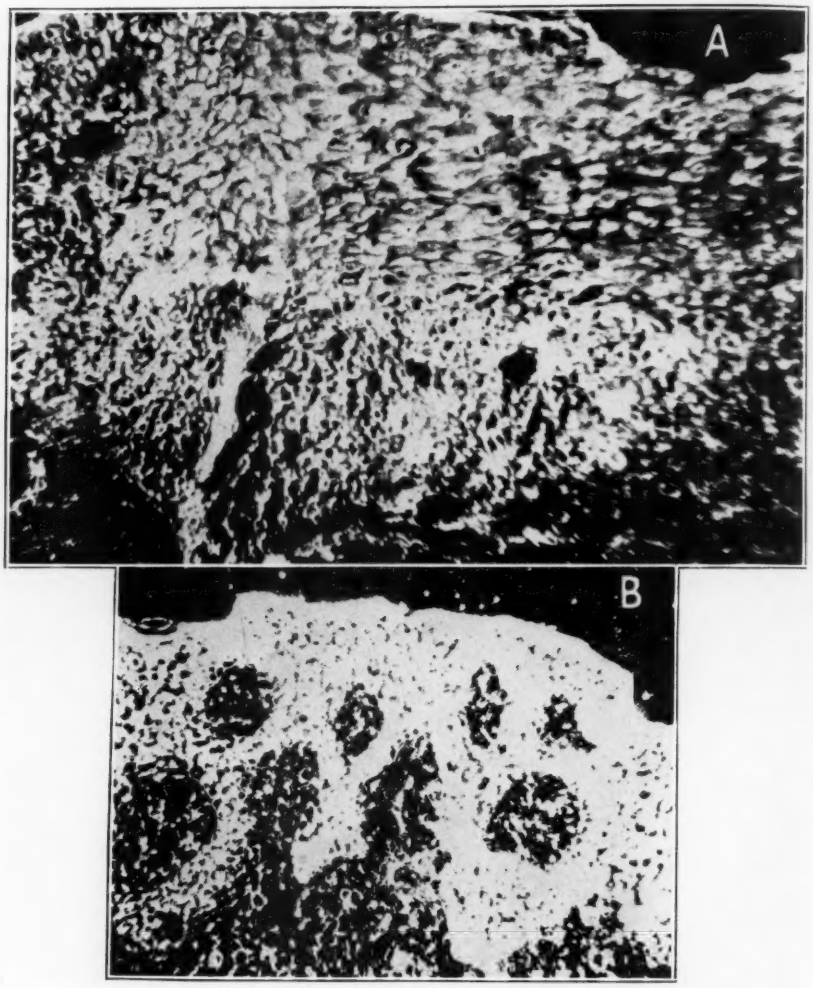

Fig. 9.—Active lesions (× 670) of (*A*) lichen planus and (*B*) psoriasis.

Contact Dermatitis (Eczema).—Six of the 8 specimens of lesions of contact dermatitis were taken from patients suffering from this dermatitis for varying lengths of time, some with the chronic form and others with the acute. The remaining 2 were from skin to which patch tests had been applied and certainly do not illustrate a chronic type of dermatitis.

The corneum in all cases of contact dermatitis is poorly mineralized with white ash of calcium and magnesium (fig. 8 *D*). In skin involved by patch test dermatitis only the corneum, granular cells and outermost

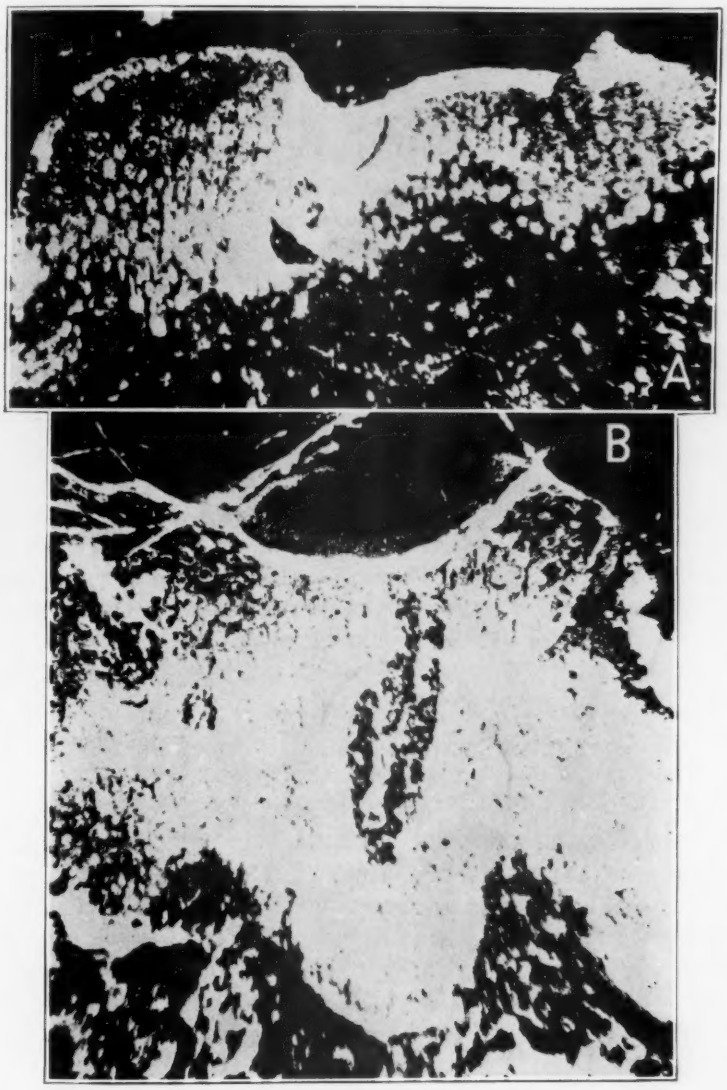

Fig. 10.—Lesions (× 900) of (*A*) xeroderma pigmentosum and (*B*) pemphigus.

spinous cells lack white ash of calcium and magnesium. The remainder of the epidermis contains either normal amounts of these elements or increased amounts. The lower two thirds of the epidermis seems undisturbed so far as the white ash is concerned, except in areas

above dermis which is infiltrated with many invading monocytes and fibroblasts, where the spinous cells and basal cells are filled with white ash.

In some cases of chronic contact dermatitis most of the spinous cells as well as the corneum lack white ash of calcium and magnesium. There is in every case, however, a layer of spinous cells next the basal layer which are heavily mineralized with white ash. The nuclei of the spinous cells of the outer epidermis contain little white ash, but those of the deeper cells appear normal in their ash content.

Lichen Planus.—Although we had only 1 specimen of this disease, its ash content is an interesting contrast to that of active lesions of neurodermatitis. The whole epidermis of lichen planus skin is heavily loaded with white ash, and the dermis is filled with infiltrating blood and connective tissue cells that are likewise filled with white ash (fig. 9*A*). The dermis and epidermis are so similarly filled with white ash that the border of the basal cell layer of the epidermis is not easily identified in ashed sections.

Psoriasis.—All that we wish to state about the ashed sections (fig. 9*B*) of psoriasis skin is that most sections of active lesions of this disease did not incinerate completely at the same temperature and speed of incineration as did sections of active lesions of neurodermatitis on the same slides with sections of psoriasis lesions. Sections of psoriasis lesions left much troublesome carbon on the slides after incineration. We intend to describe these sections in a later paper.

Xeroderma Pigmentosum.—It is interesting to note that in heavily pigmented areas in xerodermatous skin only the corneum leaves much white ash, while in nonpigmented areas the whole epidermis contains much white ash of calcium and magnesium (fig. 10*A*).

Pemphigus.—In pemphigus there are large masses of white ash accumulated around the many vesicles in active lesions (fig. 10*B*). This white ash consists largely of doubly refractive granules of silicon. The surrounding epidermis leaves ash that is similar to normal epidermis, except that it contains a large amount of organically bound iron both in the nuclei and in the cytoplasm. The outer third of the dermis is filled with a white ash that is filled with much silicon that seems to have been mobilized from the deeper part of the dermis.

HISTOCHEMICAL CHANGES DURING DEVELOPMENT OF A NEURODERMATITIS LESION

A cutaneous lesion in neurodermatitis apparently develops simultaneously with important histochemical changes in the following manner: In an already magnesium-deficient hyperpigmented unaffected area of the skin, the proteins of the spinous cells become so altered that they are unable to bind and retain biologically sufficient quantities of calcium

and magnesium proteinates. The spinous cells accumulate large amounts of inactive storage iron in its inorganic state, which apparently cannot be manufactured by this abnormal skin into active organic iron compounds. Nearly all trace of intranuclear silicon is lost from the epidermal cells, although there is a store of silicon in the dermis. The spinous cells and the intercellular canals contain much sodium and potassium and but little calcium and magnesium. While all these changes are proceeding, the hyperpigmented basal cells suddenly become pigmentless as the epidermis thickens by acanthosis and hyperkeratinization. An active lesion is almost completely formed before much inflammatory perivascular infiltration is evident in the dermis; this suggests that the epidermis is the site of the primary reaction in this disease rather than the blood vascular system, as some have believed. The whole epidermis in the area of a developing lesion finally becomes so filled with extracellular fluids, containing much sodium and potassium, that individual epidermal cells imbibe water and disintegrate completely.

On healing, the proteins of the epidermis evidently regain their original properties, and calcium and calcium and silicon are retained in large quantities, although the magnesium content is still markedly diminished. The iron in healing lesions is for the most part active organically bound iron in contrast to the inorganic iron in the active lesions. During the healing process, the skin regains its ability to manufacture usable organic iron from its stores of inorganic iron. It probably absorbs new already formed organic iron from intercellular fluids.

Thus, a neurodermatitis lesion is formed on an abnormal matrix that is hyperpigmented and deficient in magnesium as well as lacking in biologically active iron. The reasons for such abnormalities are of course entirely unknown. The uniform constancy of the marked deficiency of magnesium in the skins of patients with neurodermatitis has led us to suspect that this disease represents the striking syndrome of magnesium deficiency so easily induced experimentally in animals. But certainly lack of magnesium is not wholly to blame. Melanin slowly accumulates in enormous quantities in unaffected skin and then suddenly breaks down at the onset of a lesion. Such sudden melanolysis must release toxic amounts of free sulfur or sulfhydril compounds into the epidermis which must be bound quickly into keratin. Hyperkeratinization does not occur as rapidly as does melanolysis in a developing active lesion. If not bound quickly enough, sulfides may on contact with certain proteins form and injure the protoplasm. Deposition of melanin in the skin is undoubtedly related to the functioning of the adrenal gland, since this pigment accumulates in the skin after disorders of the adrenal organ such as occur in Addison's disease.

The lack of active organic iron in unaffected skin and lesions probably influences normal oxidative reactions, so that other oxidative mechanisms

may be overburdened with metabolic tasks. That this lack of active iron is not related to the lack of magnesium is shown by the fact that in healing lesions active organic iron is recovered in the absence of magnesium. Calcium is lacking in the spinous cells of active lesions, and it varies greatly in amount in other parts of the skin. The fragmentary evidence available shows that calcium is precipitated and deposited in abnormally large amounts in soft tissues in magnesium-deficient animals.[16] In neurodermatitis calcium is shifted from the epidermal cells to the corneum and dermis. In many patients with neurodermatitis cataracts develop as a result of deposits of calcium in the lenses.[17]

THE POSSIBLE ROLE OF SILICON

Silicon is universally present in animal tissues.[18] This seems to indicate that it is at least a constant if not an essential component of protoplasm. It has been studied largely in pathologic tissues. It apparently induces fibrosis in pathologic growths, such as scar tissue. Silicon is almost always present in large amounts in ulcerative lesions, such as those of tuberculosis. In pemphigus this element seems to be involved in the formation or healing of a vesicle, for it is present in great masses around a lesion. Little is known of the biologic function of silicon.

In neurodermatitis intranuclear silicon is evidently associated with the healing process. During the stages of development of an active lesion silicon is lost from the spinous cell nuclei, while during the healing of a lesion intranuclear silicon is recovered. The loss of silicon is concomitant with depigmentation in an active lesion, and the recovery of it, with repigmentation in healing lesions. Excess silicon in the dermis of unaffected skin may account for fibrosis in unaffected skin of patients with neurodermatitis.

THE NATURE OF IRON IN NEURODERMATITIS

Normal skin contains small quantities of masked organic iron that is biologically active. In unaffected skin and active lesions of neurodermatitis the iron for the most part is present in an inorganic storage form that is not readily available for metabolism, while in healing lesions of this disease nearly all of the iron is bound into some organic compound, such as cytochrome, that is biologically active. A large proportion of the inorganic iron in active lesions is located in the nuclei

16. Moore, L. A.; Hallman, E. T., and Sholl, L. B.: Cardiovascular and Other Lesions in Calves Fed Diets Low in Magnesium, Arch. Path. **26**:820 (Oct.) 1938.

17. Brunsting, L. A.: Atopic Dermatitis (Disseminated Neurodermatitis) of Young Adults, Arch. Dermat. & Syph. **34**:935 (Dec.) 1936.

18. King, E. J., and Belt, T. H.: The Physiological and Pathological Aspects of Silica, Physiol. Rev. **18**:329, 1938.

and perinuclear cytoplasms of the spinous cells. The inorganic iron appears to have been metabolically inactive in unaffected skin and active lesions and cast off with the keratin of the corneum. During the healing processes, either the already present inorganic iron becomes bound into biologically active organic compounds or the regenerating epidermis is enabled to absorb "masked" organic iron from the surrounding extracellular fluids and to retain it as such.

The complete history of the metabolism of iron with its fabrication into organically useful compounds has not yet been revealed. Normal skin stores inorganic iron that is probably available for the formation of hemoglobin and other compounds of iron. The importance of iron in the skin is attested by the tenacity with which it holds this element. Neurodermatitis skin possesses enormous quantities of inorganic iron that cannot be used. Some mechanism which governs the metabolism of iron is evidently altered, so that iron is piled up in a useless state as more and more of it is transported to the skin. Whether the inorganic iron is manufactured into active compounds by the skin itself or whether such organic compounds are brought to the skin is not known. Neurodermatitis skin may simply be unable to retain organic iron transported to it. Only during healing of lesions does the skin contain sufficient amounts of organic "masked" iron.

SUMMARY AND CONCLUSIONS

The mineral content of specimens of skin from 83 normal persons, 33 patients with chronic disseminated neurodermatitis and 55 patients suffering from other inflammatory diseases of the skin was studied by microincineration.

The ash content of normal skin fluctuates between hypermineralization and hypomineralization in children until about the age of 10 years, when a definite change toward hypermineralization begins and proceeds slowly unbroken until old age. The epidermal cells of normal skin contain much white ash of calcium and magnesium. Silicon is present in the nucleoli of all cells.

The primary mineral change in old age appears to be a shift of calcium and magnesium from the deeper part of the epidermis to the corneum and the dermis. The nuclear contents do not incinerate well at the same temperature as do nuclei of young skin. Silicon is decreased in amount.

In incinerated active lesions of neurodermatitis skin, the spinous cells contain very little calcium and magnesium and their nuclei lack silicon. This loss of minerals is concomitant with a change in the staining capacity of these cells and precedes the development of perivascular infiltrations.

Because of the lack of magnesium in the spectrograms of whole skin and the lack of white ash in the spinous cells in active lesions, it

is believed that the spinous layer contains less magnesium than any other part of the skin.

The lack of white ash of calcium and magnesium in the distal cytoplasm of basal cells in active lesions and the presence of huge bulks of it in the proximal cytoplasm of these cells suggest that calcium and magnesium are absorbed through the proximal surface of the basal cell.

The site of the primary reaction in the development of a lesion in neurodermatitis is believed to be located in the spinous cells.

The ash residue of incinerated sections of active lesions of localized neurodermatitis skin differs markedly from that of chronic disseminated neurodermatitis in that there is a mobilization of calcium and magnesium to the spinous cells rather than a loss of these elements, as in chronic disseminated neurodermatitis.

In incinerated unaffected skin conspicuously few spinous cells contain as much white ash of calcium and magnesium as in normal skin. Most of the spinous cells leave a bluish ash indicative of the presence of potassium and sodium, while some isolated cells and small groups of cells are packed with dense deposits of white ash.

Incinerated sections of unaffected neurodermatitis skin exhibit a characteristic patchwork of a bluish ash background and poorly mineralized spinous cells with scattered spinous cells, isolated and in groups, that are richly mineralized with white ash. The nuclei contain silicon.

Incinerated sections of healed neurodermatitis lesions show that the spinous cells recover white ash. The nuclei contain much silicon.

A cutaneous lesion in chronic disseminated neurodermatitis probably develops in the following manner: A physicochemical change in the proteins of the already magnesium-deficient unaffected skin is concomitant with, if not prior to, a loss of calcium and magnesium from the spinous cell.

Intranuclear silicon either is lost or fails to be absorbed in active lesions. During the healing process the spinous cells evidently regain their ability to retain biologically sufficient quantities of calcium, magnesium and intranuclear silicon.

Silicon is evidently associated with the development and abatement of a neurodermatitis lesion.

Most of the iron in normal skin from normal persons is retained in a biologically active organic state. In unaffected skin and active lesions of patients with neurodermatitis, almost all of the iron is in the inorganic storage form. Healed lesions regain large amounts of organically bound active iron.

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MULTIPLE BASAL CELL EPITHELIOMAS ORIGINATING FROM CONGENITAL PIGMENTED BASAL CELL NEVI

THOMAS W. NISBET, M.D.
PASADENA, CALIF.

In 1932 Nomland [1] presented a unique case under the same title as that of this paper. Since that time no similar cases have been reported in this country, although the French literature contains reports of at least 2 cases which appear to belong in the same category. The present report deals with a case which undoubtedly belongs in this group.

REPORT OF A CASE

History.—W. A., a woman aged 24, single, a housemaid, in otherwise excellent health, consulted me on Jan. 2, 1936 because of three small ulcerative lesions which had been present on the face for the previous twelve years. She stated that multiple "moles" had been present on the trunk and face as long as she could remember. Her mother had told her that the first "mole" had appeared on the abdomen when the patient was 2 years of age. At the age of 12 years she was taken to a physician because of the lesions on the face. Several of these had ulcerated and showed no inclination to heal. The ulcerated lesions were treated several times by electrocoagulation, the actual cautery and arsenical paste. After each type of therapy the lesions had promptly recurred.

Examination.—On examination a striking picture was revealed. Scattered over the face and involving particularly the right side of the nose and the lower eyelid (fig. 1) were several small pea-sized to large bean-sized yellow to yellow-brown pigmented lesions, any one of which considered alone would have been regarded as an ordinary pigmented mole. One of the small lesions on the face was about 5 mm. in diameter and was only slightly pigmented. This lesion presented a definite pearly border. Three larger, ulcerative lesions were also present. These lesions were the ones which had received previous treatment.

On the back (figs. 2 and 3) there were more than one hundred and fifty raised nodular tumor masses. These were entirely discrete and presented the appearance of ordinary nevi. They ranged from 2 mm. to 1.5 cm. in diameter and varied greatly in shape and color. Some were darkly pigmented, others were light brown and some were practically the color of normal skin. Some were raised slightly above the surface of the skin, while others were definitely pedunculated.

A specimen for biopsy was taken from one of the ulcerated lesions on the nose. One of the larger pedunculated lesions on the back was excised by actual cautery.

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1. Nomland, R.: Multiple Basal Cell Epitheliomas Originating from Congenital Pigmented Basal Cell Nevi, Arch. Dermat. & Syph. **25**:1002 (June) 1932.

Fig. 1.—Multiple basal cell epithelioma.

Fig. 2.—Multiple basal cell epithelioma.

Biopsy.—A specimen of the facial lesion consisted of a small skin-covered fragment of tissue 9 by 7 by 5 mm., which had a slightly brown tinge. The skin on the surface was smooth. The specimen was cut into several pieces and sectioned. One portion showed in the center a large follicle in the cutaneous surface,

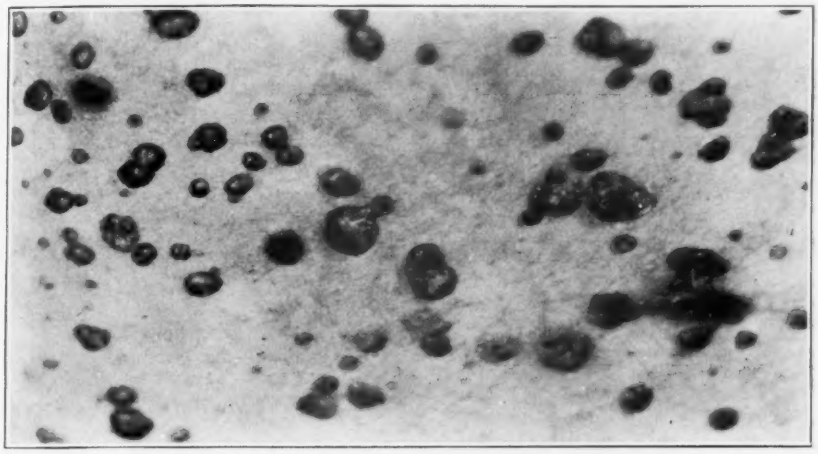

Fig. 3—Multiple basal cell epithelioma.

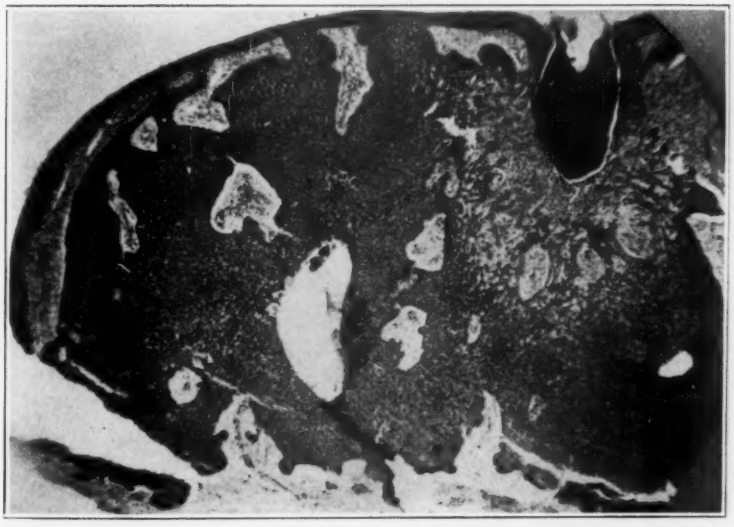

Fig. 4.—General architecture of the lesions, e. g. like that of basal cell epithelioma.

filled with desquamated epithelium and debris, and arising from the epithelium lining there was an epithelial new growth which extended widely throughout the underlying dermis. The cells immediately adjoining the follicle were somewhat elongated or polyhedral and showed ovoid nuclei and rarely a mitotic figure. These in turn connected with portions which were made of almost solid sheets

of fairly deep-staining cells which here and there were connected with the basal layers of the epidermis. These cells were fairly uniform in size and showed ovoid nuclei and a small amount of hardly visible cytoplasm, and the extreme peripheral cells in these sheets or nests were fairly similar to those of the basal layer of the epidermis. Scattered mitotic figures were seen in this cellular part of the new growth. These cells were similar to those seen in so-called basal cell tumors. An occasional pigmented stellate or oval cell was seen in the dermis in the connective tissue. Other sections showed irregular nests of similar cells connected by narrow strands, occasionally with a somewhat filigree appear-

Fig. 5.—Changes which are more infiltrative and cancer cells of transitional type (specimen from same site as that in fig. 4).

ance. In some of these nests there were a few small spaces containing fine precipitate. Here and there an occasional tumor cell showed brown pigment. The diagnosis was basal cell epithelioma.

Two specimens were removed from the back on Oct. 13, 1938. One piece was 10 by 8 by 4 mm. and the other 8 by 6 by 4 mm. Smooth epidermis covered the surface of each, except for one end. The larger piece showed a thin epidermis, the under surface of which was smooth, and extending from it in numerous places were seen varying-shaped tongues and strands of epithelium which formed throughout the entire piece a bizarre pattern. A filigree lacework was produced in some parts, and strands in these portions were only two to four

Fig. 6.—Photograph showing filigree pattern.

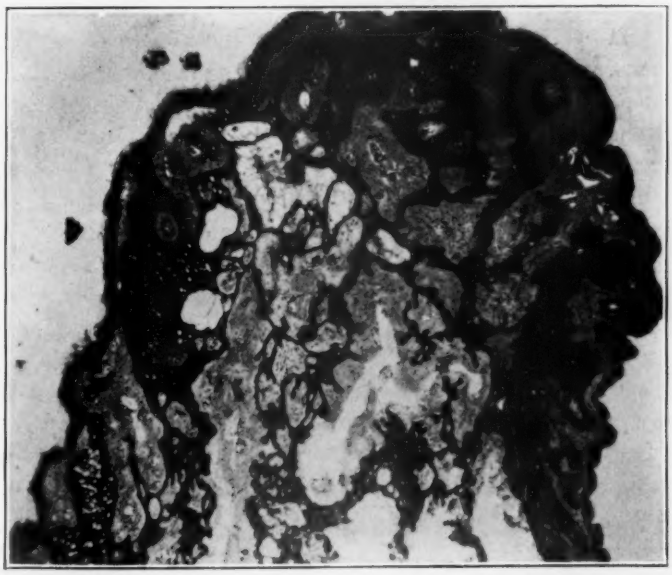

Fig. 7.—Nevus-like pattern of cells at the bottom of biopsy specimen shown in figure 6.

layers thick. Other portions showed large sheets which were composed of cells resembling so-called basal cells, with round or ovoid nuclei, which stained fairly deeply. A few mitoses were present. Also, in the larger nests of cells many small cystlike pockets were seen, containing fine threads of precipitated material, either fibrin or protein. These portions varied greatly in size, and some were as much as 0.3 mm. across. At one edge there was a large distended follicle, about 3 mm. wide with an opening 1 mm. across. This was filled with desquamated keratinized epithelial cells, a plug of which extended through the opening. The lining of this pocket was made of a thinned-out layer of squamous cells resembling that of the epidermis, and connecting with it were seen strands of the tumor cells, forming the bulk of the growth. A few pigmented cells were found in the stroma, particularly under the epidermis. The diagnosis was basal cell epithelioma, adenoidocystic type.

The smaller piece likewise showed a thin epidermis from which arose a tumor which produced a lacework-like pattern. Also, some irregular sheets of fairly densely staining basal cells were seen. In many of the nests there were small cystic pockets containing precipitated protein. In the center of the growth was a large space, over 1 mm. long, lined by epidermis-like stratified squamous epithelium and containing desquamated epithelium and debris. The diagnosis was basal cell epithelioma, adenoidocystic type.

REVIEW OF LITERATURE

The multiplicity of lesions and their clinical resemblance to ordinary nevi would seem to place this case in the same group as that of Nomland. Nomland's patient, a woman aged 38, presented numerous pigmented moles on the face and neck. They had been present as long as the patient could remember. However, all of the moles had remained quiescent until she was 28 years of age. Microscopic examination of lesions that were clinically nevi revealed the picture of a basal cell epithelioma. Other lesions suggesting molluscum contagiosum revealed a similar picture. One lesion that was clinically a basal cell epithelioma showed microscopically a somewhat different type of basal cell growth.

There is a more or less striking resemblance of the photographs of Nomland's patient to the one reported on here. Nomland made no mention of the presence or absence of lesions on the trunk.

In 1934 Weill [2] presented a woman aged 34 who had numerous small shiny unbilicated pea-sized and larger nodular lesions on the face. These involved particularly the lower eyelids and the nasolabial folds. No histologic confirmation of the diagnosis was obtained. Pautrier, who saw this patient, remarked on the resemblance of this patient to the one reported on by him in 1927. In view of Savatard's criticism of Nomland's paper one cannot accept Weill's case as belonging to this group. It may well have been a case of epithelioma adenoides cysticum of Brooke.

2. Weill, G.: Polymorphous Cutaneous Epitheliomatosis Developing During a Period of Fourteen Years, Bull. Soc. franç. de dermat. et syph. **41**:1789, 1934.

In 1936 Vigne [3] reported the case of a 22 year old girl with multiple epitheliomas of the face which first appeared at the age of 12 years. These lesions also involved particularly the lower eyelids, the inner canthi of the eyes, the nasolacrimal folds and the bridge of the nose. Many of these lesions had received previous treatment, which consisted of either curettement or cauterization. About the peripheries of those which had been curetted numerous small nodules developed. The original lesion likewise reappeared. One medium-sized pagetoid type of epithelioma was present in the right sacroiliac region, but the thorax, abdomen, arms and legs were free.

The five photographs of the face of this patient strongly resembled figure 1. Vigne's patient was observed and treated over a period of ten years. In spite of extensive electrothermal therapy recurrences in and about the scars were observed and many new lesions continued to appear. Vigne apparently had the greatest difficulty in treating the lesions about the eyelids. Numerous specimens for biopsy were taken at various times, and all revealed basal cell epithelioma but of different histologic structure.

The patient in the case of Pautrier and Archambault [4] was an embroidery worker aged 56. More than two hundred lesions were present, distributed over the entire body, face, neck, chest, dorsal and lumbar regions, back and hip. Numerous lesions were present on the upper part of the face, particularly around the eyes and near the hair line on the forehead. All of these tumors had developed over a period of twenty-three years, and in spite of their almost unbelievable multiplication they remained benign and showed no evidence of metastasis. Nor was the patient's health in any way affected. Clinically the lesions simulated nevi, Bowen's disease, eczema figuratum, psoriasis and tertiary syphilid.

Histologically five different types were present, all of the benign basal cell type. One, however, differed in appearance from anything seen previously.

COMMENT

All of these cases present many similarities. The onset of the condition is usually early in life, with activity of some of the lesions first occurring about the time of puberty. All of the patients have been female. In each instance the clinical resemblance to pigmented nevi

3. Vigne, P.: Multiple Cutaneous Epitheliomatosis Developing During a Period of Twenty Years, Bull. Soc. franç. de dermat. et syph. **43**:869, 1936.

4. Pautrier, L. M., and Archambault, S.: Extraordinary Case of Cutaneous Epitheliomatosis: More Than Two Hundred Epitheliomatosis Foci Developing During Twenty-Three Years on Various Parts of the Skin Without Constitutional Symptoms and Presenting Five Histologic Types, Bull. Assoc. franç. p. l'étude du cancer **16**:835, 1927.

has been striking. There is uniformity among all observers that when the lesions are inadequately treated recurrence is unavoidable. It is then that the borders of such recurrent lesions take on the clinical appearance of basal cell epithelioma. When left alone they seem to persist in a more or less quiescent state. In no case has any metastasis been reported. In every case there have been large numbers of lesions of extreme variations in form and color. In all cases the face has been involved. The present case is the only one in which numerous lesions were present on the chest, abdomen and back (excepting possibly Pautrier's case).

Without going into detail as to the characteristics of cylindromas of the scalp, I may state that it seems likely from a consideration of that disease that the epitheliomatous disorder under consideration bears the same relationship to epithelioma adenoides cysticum as cylindroma does. In fact, as early as 1904 Hartzell [5] made the statement that cylindroma of the scalp, multiple benign epithelioma (epithelioma adenoides cysticum) and syringoma were all varieties of trichoepithelioma. In none of the cases of the present disorder was any mention made of any lesions on the scalp. Nevertheless, involvement of the face by epithelioma adenoides cysticum is not uncommon in cylindroma of the scalp.[6]

Shortly after the publication of Nomland's paper, Savatard,[7] in a communication to the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY, suggested that Nomland's case was one of epithelioma adenoides cysticum. He felt that Nomland had unjustly excluded this diagnosis on the grounds "that this condition is always a familial disorder," that it never undergoes epitheliomatous degeneration and that the lesions are necessarily nonpigmented.

Nomland [8] in a reply to Savatard defended his position and cited additional reasons for not believing his case to be one of an unusual variant of epithelioma adenoides cysticum (Brooke). He stressed again the familial occurrence of this disease and stated that epitheliomatous degeneration was exceedingly rare, that pigmented lesions were usually few and that the pathologic picture in the two diseases was entirely different.

Cases similar to that of Nomland [1] with the publication of additional certain facts might be gathered which support Savatard's position. The

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5. Hartzell, M. D.: Trichoepithelioma and Cylindroma, Brit. J. Dermat. **16**: 361, 1904.

6. Stillian, A. W.: Nevo-Epithelioma Adenoides (Cylindroma) of the Scalp, Arch. Dermat. & Syph. **27**:481 (March) 1933.

7. Savatard, L.: "Multiple Basal Cell Epitheliomas Originating from Congenital Pigmented Basal Cell Nevi," correspondence, Arch. Dermat. & Syph. **26**:589 (Sept.) 1932.

8. Nomland, R., in reply to Savatard.[7]

first is that in all of the reported cases the patients have been young women, although in no case was there any history of a familial tendency. Secondly, in all of these cases, including Nomland's, the areas of predilection have been the same as found in epithelioma adenoides cysticum, usually the lower eyelids, the nose and portions of the cheeks immediately adjacent to the nose. The similarity of the facial involvement, judging from photographs which have been published, including those of the present case, is striking. In fact, the facial expression of the patients are so similar that one might believe all of them related to each other except for the different countries of birth.

The title chosen for this paper was taken from Nomland's paper not because an origin from nevi was accepted but rather in an attempt to group all cases of this kind under one heading. Only in this manner can the correct nosologic position be eventually ascertained. In fact, the development of the disease in early life is suggestive that this type of epithelioma is of nevoid origin but not necessarily arising from pigmented nevi. Clinically the untreated lesions certainly have the gross appearance of pigmented nevi. Microscopically these lesions surely are not pigmented nevi in the ordinary sense that this term is used. Certainly no true nevus cells are present, and there is nothing to indicate an origin from nevus cells, such as the cell nest or cell strands. Microscopically whether the tissue is removed from a quiescent lesion or from one that is apparently actively proliferating, the histologic picture is one of basal cell epithelioma. This picture is of course variable as to the exact type. However, in no reported case has the published photomicrograph resembled the histologic picture which is ordinarily accepted as characteristic of epithelioma adenoides cysticum. This fact was pointed out by Nomland, and the cases published since his article certainly tend to verify this fact.

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ACROSCLEROSIS

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The syndrome acrosclerosis combines the features of Raynaud's phenomena with a characteristic scleroderma of the distal parts of the extremities and of the face and neck. Apparently there is much confusion among dermatologists regarding the clinical nature of acrosclerosis and its differentiation from diffuse scleroderma as well as from other forms of sclerodactylia and even from Raynaud's disease. To clarify some of the diagnostic and prognostic essentials of acrosclerosis is the purpose of this paper.

Historically it may be pointed out that Raynaud himself identified the association of acral cutaneous sclerosis with the vasomotor symptoms which bear his name.[1] During the years that followed other authors perceived the same relation. Appolinario,[2] it is recorded, early insisted that the combination of scleroderma and local asphyxia of the extremities indicated not the presence of two superposed diseases but a complex form of a single disease. A half-century ago Hutchinson[3] described, under the designations of "acro-scleroderma" and "acroteric morphea," further examples of this vasomotor form of scleroderma. In 1893 he wrote in detail of *acrosclériase,* describing its typical onset in the extremities, its tendency to spare the trunk and the accompanying vasomotor symptoms which established the relation to Raynaud's disease.

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* From the Section on Dermatology and Syphilology, the Mayo Clinic.

1. (*a*) Raynaud, M.: On Local Asphyxia and Symmetrical Gangrene of the Extremities, translated by T. Barlow, London, The New Sydenham Society, 1888, vol. 121, pp. 66-70. (*b*) Ball: Rapport de la commission des maladies Régnantes, Bull. et mém. Soc. méd. d. hôp. de Paris **8**:59-61, 1871.

2. Appolinario, cited by Castellino and Cardi.[4]

3. Hutchinson, J.: Inherited Liability to Raynaud's Phenomena, with Great Proneness to Chilblains—Gradual Increase of Liability to Paroxysmal Local Asphyxia—Acro-Sphacelus with Scleroderma—Cheeks Affected, Arch. Surg., London **4**:312-313 (April) 1893; De l'acropathologie; maladie de Raynaud, et états similaires, Semaine méd. **13**:109-110, 1893; On Morphoea and Allied Conditions, Arch. Surg., London **6**:350-367 (Oct.) 1895; Acro-Scleroderma Following Raynaud's Phenomena, Clin. J. **7**:240 (Feb. 5) 1896.

The publications of Castellino and Cardi,[4] Cassirer [5] and Cassirer and Hirschfeld [6] give further and detailed consideration to the problem. It has been our objective not to summarize the extensive literature which we have surveyed but merely to sketch part of the historical background of acrosclerosis. It may be stated here that review of the literature reveals acrosclerosis—although still a subject of doubt and debate among dermatologists—to have long been identified and segregated as a distinct entity by many able students of vascular diseases.

Sellei,[7] beginning in 1931, called to the attention of dermatologists the clinical picture recognized by Hutchinson, made known the name acrosclerosis and vigorously championed the status of acrosclerosis as a disease *sui generis*. One of us (O'Leary) had the opportunity in 1935 to examine personally the patients presented by Sellei in Budapest and confirmed that acrosclerosis made up a distinctive syndrome, which had been observed among patients at the Mayo Clinic. We wish to make clear our view that acrosclerosis is by no means a "new" disease, that its recognition is not difficult once the typical course and features have been pointed out and that its differentiation from other forms of scleroderma establishes it as a definite clinical entity.

CLINICAL FEATURES

Data on 64 cases observed at the Mayo Clinic of a condition combining the manifestations of Raynaud's disease and sclerosis of the extremities and face have been reviewed for this study. The sex distribution and the age at onset are given in table 1.

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4. Castellino, P. F., and Cardi, G.: Sulla gangrena simmetrica delle estremità (malattia di Raynaud), Morgagni **37**:625-677 and 689-729, 1895.

5. Cassirer, R.: Die vasomotorisch-tropischen Neurosen, ed. 2, Berlin, S. Karger, 1912.

6. Cassirer, R., and Hirschfeld, R.: Vasomotorisch-tropische Erkrankungen, in Kraus, F., and Brugsch, T.: Spezielle Pathologie und Therapie innerer Krankheiten, Berlin, Urban & Schwarzenberg, 1924, vol. 10, pt. 3, pp. 559-591 and 622-655; Vasomotorisch-tropische Erkrankungen, in Bumke, O., and Foerster, O.: Handbuch der Neurologie, Berlin, Julius Springer, 1935, vol. 17, pp. 246-281 and 312-366.

7. Sellei, J.: Die Akrosklerosis (Sklerodaktylie) und deren Symptomenkomplex nebst neueren Untersuchungen bei Sklerodermie, Arch. f. Dermat. u. Syph. **163**:343-365, 1931; Sklerodermie und Schleimhaut, ibid. **170**:464-466, 1934; The Diagnosis and Treatment of Scleroderma and Acrosclerosis, and Some of Their Kindred Diseases, Brit. J. Dermat. **46**:523-536 (Dec.) 1934; L'acrosclérose (sclérodactylie, sclérodermie progressive syndromes angiospasmodiques trophiques de la face et des mains) la sclérodermie vraie et la maladie de Raynaud, Ann. de dermat. et syph. **7**:829-839 (Sept.) 1936; Zur Differentialdiagnose der Akrosklerose (Angiospastische-trophische Veränderungen des Gesichts und der Hände) und der Raynaudschen Krankheit, Arch. f. Dermat. u. Syph. **173**:352-356, 1936.

The early symptoms, in the majority of instances, are those due to intermittent arteriolar spasm in the upper extremities—a series of events characterized successively by pallor, cyanosis and rubor—identical with the phenomena of Raynaud's disease.[8] The sclerosis which occurs in acrosclerosis may occasionally appear contemporaneously with the vasomotor symptoms or, more commonly, at a variable interval afterward, which may be as long as twenty years. Sclerosis of the toes and feet appears in a minority of cases, and it is a curious fact that, even though the feet may occasionally be the site of classic Raynaud's phenomena, they can escape involvement by scleroderma altogether. The onset of facial sclerosis either coincides with the appearance of sclerodactylia (12 cases) or it appears afterward, sometimes not being noticeable for as long as ten years after the onset of the sclerodactylia. Often our patients were not aware of the facial involvement until attention was directed to it in the course of an examination. The occurrence of

TABLE 1.—*Age and Sex Incidence of Acrosclerosis*

Age at Onset, Years	Women	Men
10-19	10	..
20-29	16	4
30-39	20	1
40-49	6	3
50-59	3	..
60+	1	..
Total	56	8

vasomotor abnormalities of the face is not common, only 3 patients reporting the appearance of cyanosis of the nose or lips on exposure to cold.

A composite clinical picture of a patient suffering from acrosclerosis, as drawn from a review of our cases, would appear as follows: Over the fingers and hands the skin is smooth, shiny or waxy, and tense (fig. 1). The color is pale, dusky pink or cyanotic, or a mottling of shades may be present. The fingers appear stiff and sometimes slightly swollen and are maintained in semiflexion. The terminal phalanges are either tapering or rounded, and the integument of this part is rubbery or board hard and bound fast to the underlying structures. The skin of the fingers shows a progressive decrease of induration proximally. Over the dorsa of the hands the skin may appear to be normal, but efforts to pick it up yield only small folds, indicating the essential sclerotic state. The change is present over the wrists and often up the forearms in a diminishing degree toward the elbow (seldom does it extend beyond), where it merges gradually with the normal skin.

8. Raynaud's "syndrome" is possibly a more accurate expression. The contribution of Hunt [32] adequately discusses this phase of terminology.

The hands and fingers usually are cool and moist, and the firm finger tips exhibit dystrophic changes, such as scaling, fissuring, keratosis or depressed scarring. Small, painful, indolent ulcers or dark crusts appear under the edge of the nail and on the finger pad, or suppuration occurs about the wall of the nail. Calcareous concretions [9] may be present as yellowish nodules under the skin (8 cases), which at times discharge their chalky contents mixed with purulent secretion. The nails show the effects of impaired nutrition, appearing thick, beaked, rough and lusterless or as thin, shrunken, deformed plates. Excoriations, fissures and ulcers may develop on the knuckles. Abnormal

Fig. 1.—The typically tense, smooth skin over the fingers and hands is shown. Significant features include clubbing of the nails, shortening of the terminal phalanges and scars over the proximal interphalangeal joints.

changes in color with dependency and elevation do not occur, nor are the arterial pulsations at the wrist impaired. Occasionally gangrene en masse of a phalanx may occur (fig. 2 *a*), necessitating amputation; this has occurred in 3 of our cases.

Dystrophic cutaneous changes analogous to those on the fingers and hands may be found on the feet and toes, but in the majority of cases

9. Garcin, R.; Bertrand, I.; Laudat, M., and Cachin, C.: Concrétions calcaires sous-cutanées des doigts associées à un syndrome de Raynaud avec sclérodactylie. Télangiectasies disséminées, Bull. et mém. Soc. méd. d. hôp. de Paris **1**:1036-1045 (June 22) 1931.

they are, fortunately, lacking. When present, they do not assume the same degree of severity as those of the upper extremities.

The skin on the face becomes drawn and stretched so that the lines of expression are smoothed out (figs. 2 *b* and 3), producing typically a "bland" physiognomy. As Sellei pointed out, the skin is not so hard as it is taut, as though it were shrunken. This is an important observation. The cheeks are always affected, the skin appearing to be stretched over the sides of the face, but the forehead sometimes is uninvolved. The lower eyelids can be but slightly everted. Sclerosis obviously impedes the movements of the mouth; the lips become retracted and the vermilion borders narrowed, shortened and blanched when the mouth is opened. Often superficial radial furrows occur over the lips and the chin becomes lightly puckered. The nose assumes a sharp, "pinched" appearance. The sclerotic changes may invade the skin of the neck and that over the clavicles and the upper part of the thorax. Hyper-

Fig. 2.—A patient suffering from advanced acrosclerosis, present for about twelve years. *a*, the fingers, showing an unusual degree of mutilation due to attacks of massive gangrene, necessitating repeated amputations. Note the deformed remaining fingers, stunted nails, keratotic and necrotic plugs over the tips and dark regions of superficial necrosis on the right thumb and little finger. The dressing covers the stump of a finger recently amputated. *b*, the "ironed-out" facies, showing the taut skin, thinned lips, furrows about the mouth and on the chin, obliteration of the nasolabial and infraorbital folds and limited voluntary wrinkling of the forehead.

pigmentation occasionally supervenes, usually on the affected parts, as a diffuse or mottled discoloration. On the face small telangiectatic macules fairly frequently appear, a phenomenon also observed in other forms of scleroderma. Weissenbach, Boppe, Martineau and Malinsky [10] indicated that the distribution of telangiectases may be independent of sclerosis of the skin, but in our cases the lesions appeared only on

10. Weissenbach, R. J.; Boppe; Martineau, J., and Malinsky, A.: Sclérodermie progressive. Télangiectasies multiples disséminées. Parathyroïdectomie, Bull. Soc. franç. de dermat. et syph. **42**:1413-1417 (July) 1935.

affected parts, and nearly always on the face alone. The scalp may participate in the sclerosing process, but alopecia apparently never results.

After the development of the cutaneous changes on the hands, forearms, face and upper part of the chest, further extension is unusual, although the vasomotor phenomena persist and the sclerosis and other trophic disturbances may increase. The topographic localization or restriction is an essential feature of acrosclerosis, being one of the characteristics which distinguish it sharply from progressive diffuse scleroderma.

Roentgenologic changes have been described in the distal phalanges,[11] consisting of resorption which starts at the head of the bone and progresses proximally, leaving a shortened phalangeal stump. (It is

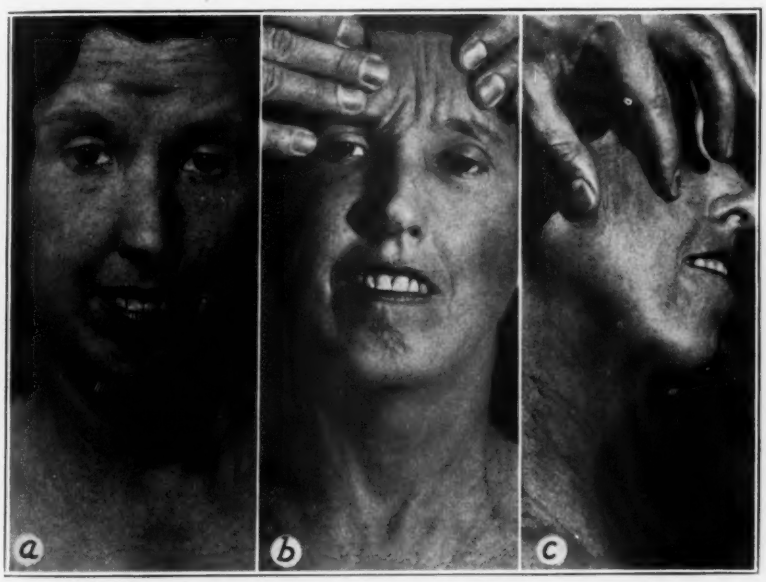

Fig. 3.—Early acrosclerosis, illustrating (*a*) the diminished mobility of the features (patient attempting to wrinkle forehead) and (*b*) sclerosis of the forehead, with decreased wrinkling on pressure. Superficial furrows are visible over the lips, and the chin is conspicuously puckered. In *c* is demonstrated the taut skin of the cheek, which resists attempts to pinch it into folds.

important to note that the shortenings may occur without the presence of cutaneous ulceration. Prinzmetal,[12] in fact, explained the osseous absorption simply by the persistent pressure of the involved skin.)

11. Bársony, T., and Frisch, E.: Beiträge zur Röntgenologie der "Akrosklerose," Fortschr. a. d. Geb. d. Röntgenstrahlen **47**:287-293 (March) 1933.

12. Prinzmetal, M.: Studies of the Mechanism of Circulatory Insufficiency in Raynaud's Disease in Association with Sclerodactylia, Arch. Int. Med. **58**:309-328 (Aug.) 1936.

Subcutaneous calcification of the finger tips in acrosclerosis (fig. 4) is a common occurrence, as contrasted with its rarity in pure Raynaud's disease. Also, fragments of bone from the distal phalangeal tip may separate and ultimately become smoothed and condensed. Roentgenologic changes do not always parallel the digital cutaneous changes, however, as 6 of 23 patients examined showed an essentially normal bony structure.

Disturbances in the large joints (elbows, shoulders, ankles and knees) were presented by fully a fourth of the patients, in several of whom the symptoms antedated the vasomotor signs. The complaint was referable, as a rule, to stiffness, aching, tenderness and sometimes swelling over the affected articulations. The pathologic process is probably localized in the periarticular tissues and in the musculature and is usually independent of scleroderma affecting the overlying skin.

Fig. 4.—Roentgenogram of the hands, the seat of Raynaud phenomena for twenty years and of sclerodactylia for about five years, with calcinosis in the finger pads. The tip of the second phalanx on the right has split off, and the fragment is undergoing condensation. Shortening of several of the distal phalanges may be observed.

Mild dysphagia occurred in 8 cases, in 2 of them there being demonstrated endoscopically cicatricial stricture of the esophagus. Sclerosis of the mucous membranes, particularly the esophageal, has been reported by Sellei, and Weissenbach, Boppe, Hoesli and Martineau [13] have described the pathologic alterations in the esophagus in such a

13. Weissenbach, R. J.; Boppe; Hoesli, H., and Martineau, J.: Sclérodermie progressive. Troubles oesophagiens. Parathyroïdectomie inférieure droite. Parathyroïdectomie inférieure gauche, un an plus tard. Mort par hématome cervicothoracique. Autopsie. Etude des lesions oesophagiennes, Bull. Soc. franç. de dermat. et syph. **45**:300-308 (Feb.) 1938.

case. One of our patients, in whom hoarseness developed during the course of the disease, showed a diffuse infiltration of the larynx, probably by the same process as that affecting the skin.

Evidence of cardiovascular disease was detected in 5 cases: mitral endocarditis in 2, hypertension with cardiac enlargement in 2 and coronary sclerosis in 1. It may be purely coincidental that in 3 other cases exophthalmic goiter developed during the course of the disease, apparently without influencing the progress in any way.

PROGNOSIS OF ACROSCLEROSIS

As stated previously, the disease characteristically progresses slowly to a definite degree and extent of sclerosis, in which form it then remains more or less stationary. The sclerosis, vasomotor phenomena and trophic changes persist, and the last two may even increase in severity. But often the reverse is true and partial regression may take place gradually, even after many years.

Follow-up observation of the group of patients studied revealed that in at least half of them arrest of the disease or satisfactory involution occurred after the scleroderma had been present for from two to twenty years. In several of them the skin had returned nearly or quite to normal, while the vasospastic manifestations were materially abated. We did not find any case in which there was a total disappearance of vasomotor abnormalities, although in some they had become quite inconspicuous.[14]

Fourteen patients in this series died, of various causes, from three to fifteen years after onset of acrosclerosis (average, seven years). Some of these patients were known to have had acrosclerosis in an arrested, nonprogressing form. We were able to determine that in 5 cases death was caused by cardiac disease and in 1 each by acute nephritis, bronchopneumonia and gangrene of a foot. Most of the deaths, we are convinced, were in no way related to the acrosclerosis. Our mortality data are too meager to serve the purpose of statistical analysis satisfactorily.

RAYNAUD'S SYNDROME WITH SCLERODACTYLIA

The fact has already been mentioned that not only may sclerosis of the fingers for years precede cutaneous changes elsewhere but Raynaud phenomena may for years precede the scleroderma. In short, sclerodactylia must be regarded as a potential complication in a case of Raynaud's syndrome, and the ultimate extent of the sclerosis may not

14. In Scolari's case (Scolari, E.: La sclerodattilia e la sclerodermia diffusa con speciale riguardo alle turbe vasomotorie. Loro rapporti con il morbo di Raynaud, Zentralbl. f. Haut- u. Geschlechtskr. **42**:470, 1932) the vasomotor phenomena disappeared entirely two years after the onset of scleroatrophic changes on the hands.

be attained until many years after its onset. Monro [15] mentioned this circumstance, and Cassirer [5] discussed its development in detail. We have studied the records of a group of 42 patients suffering from Raynaud's "disease" who presented at the time of examination cutaneous sclerosis limited to the fingers and hands. These represent approximately 10 per cent of the patients with Raynaud's disease seen at the Mayo Clinic.

Six patients were men and 36 women. The age distribution was practically identical with that given for the acrosclerotic group. Raynaud symptoms had preceded the appearance of cutaneous changes by from one to many years. The skin showed the same conditions as those of the group previously described, but in general the changes were less severe. In a third of the cases the hands were involved as well as the fingers, and, as in acrosclerosis, the degree of involvement of the skin diminished proximally, fading out gradually over the middle phalanges in milder forms of the disease and at the wrists in more extensive ones. The skin was firm, taut and often dusky; the fingers were stiff, flexed, sometimes swollen and commonly blunted at the ends. Trophic changes were visible in the deformed nails, necrotic pits, keratotic puncta, calcified nodules or scarring at the finger tips.

We believe that the pathogenesis of the sclerotic disturbance in this group of cases is similar to that in the cases of more extensive involvement described in the preceding section (acrosclerosis). Conceivably the sclerosing process may in some cases halt while the cutaneous changes are limited to the fingers or hands, just as it may in other cases halt, for whatever reasons, after the face and feet have been implicated. We propose to combine these two types under the common denomination of "acrosclerosis," restoring to the term the inclusive sense suggested by Hutchinson.

DIFFERENTIAL DIAGNOSIS

Diagnostically one must segregate a well defined group of cases in which the onset is associated with Raynaud's syndrome and in which scleroderma, appearing first over the acral parts, extends ultimately over wide regions of the body—the condition known as generalized progressive scleroderma. Acrosclerosis, we believe, has often erroneously been considered a form of this disease. Our study of 22 patients suffering from generalized progressive scleroderma indicates that the following essentials characterize it: 1. The sexes are nearly equally represented, in contrast to the preponderance of women among patients with acrosclerosis. 2. Once sclerosis begins, the course is

15. Monro, T. K.: Raynaud's Disease, Glasgow, James Maclehose & Sons, 1899.

notably progressive, and in a relatively short time (in every case within two years) the scleroderma involves the face and extremities and is widespread over the trunk. 3. The involved skin is brawny and thickened and exhibits a waxy sheen which may be sharply demarcated,

TABLE 2.—*Differential Features of Acrosclerosis and of Generalized Progressive Scleroderma*

	Acrosclerosis	Generalized Progressive Scleroderma
Sex incidence	Women preponderantly (7:1 in this series); not seen in children	Sexes nearly equally represented; occasionally seen in children
Onset	Raynaud's symptoms in every case (early symptoms often misinterpreted as "arthritis"); onset of cutaneous sclerosis usually noted in fingers	Symptoms of arthralgia, stiff joints, loss of weight, asthenia or vasomotor phenomena; onset may be any place, often trunk
Vasomotor phenomena	Raynaud's syndrome usually precedes sclerosis by months or years	Raynaud's syndrome absent at onset in edematous type; may develop secondarily later; in progressive diffuse scleroderma Raynaud features occasionally precede or appear simultaneously with onset of sclerosis and are milder
Extent of sclerosis	Sclerosis affects skin of hands, upper extremities, face, neck and upper part of chest, in this order; rarely legs are involved, but ankles and feet are usually spared; esophagus often involved	In progressive type upper and lower extremities and much of trunk frequently affected; face involved in the extensive eruptions; entire skin may become sclerosed
Type of cutaneous lesion	Classic "waxy" hidebinding not seen as in scleroderma; rarely such a patch (morphea) is noted about shoulder girdle; skin of face is tight but not waxy hard; lips thinned, nose pinched, ectropion rare; late in disease skin is less hidebound and atrophy conspicuous by its absence	Classic "waxy" firm hidebinding with cutaneous atrophy common
Course	Slow, usually over a period of many years; sclerosis restricted to the parts named, regardless of duration; gangrenous mutilation of fingers occurs; increase of pigmentation uncommon	In progressive type most of body involved within two years after onset of scleroderma; small gangrenous ulcerations of fingers, elbows, etc.; generalized hyperpigmentation common
Prognosis	Vasomotor phenomena persist for years; sclerosis may become arrested spontaneously and may regress partially; prognosis for life good; death seldom due directly to the disease	Gross mortality rate of patients with progressive type approximately three times that of patients with acrosclerosis; spontaneous remissions seldom occur
Pathogenesis (hypothesis)	Vasomotor disturbance, probable seat in cerebral centers	In ordinary diffuse scleroderma abnormality may be primary in collagen itself or may be generalized metabolic fault (calcium? tissue enzymes?) expressing itself largely through cutaneous changes

whereas the skin in acrosclerosis is softer, being taut rather than indurated and thickened, and lacks the prominent sheen of scleroderma. 4. The prognosis in this form of diffuse scleroderma is decidedly unfavorable, the gross mortality rate averaging at least three times that of acrosclerosis. An important reason for distinguishing these two conditions, therefore, is in the interest of prognostic accuracy.

The differential features of acrosclerosis and of generalized scleroderma are given in table 2.

Reference must be made also, for purposes of differential diagnosis, to instances of sclerodactylia in which vasospastic features are initially absent, although they may follow the sclerosis after months or years (in approximately a fourth of the cases). The areas affected may be

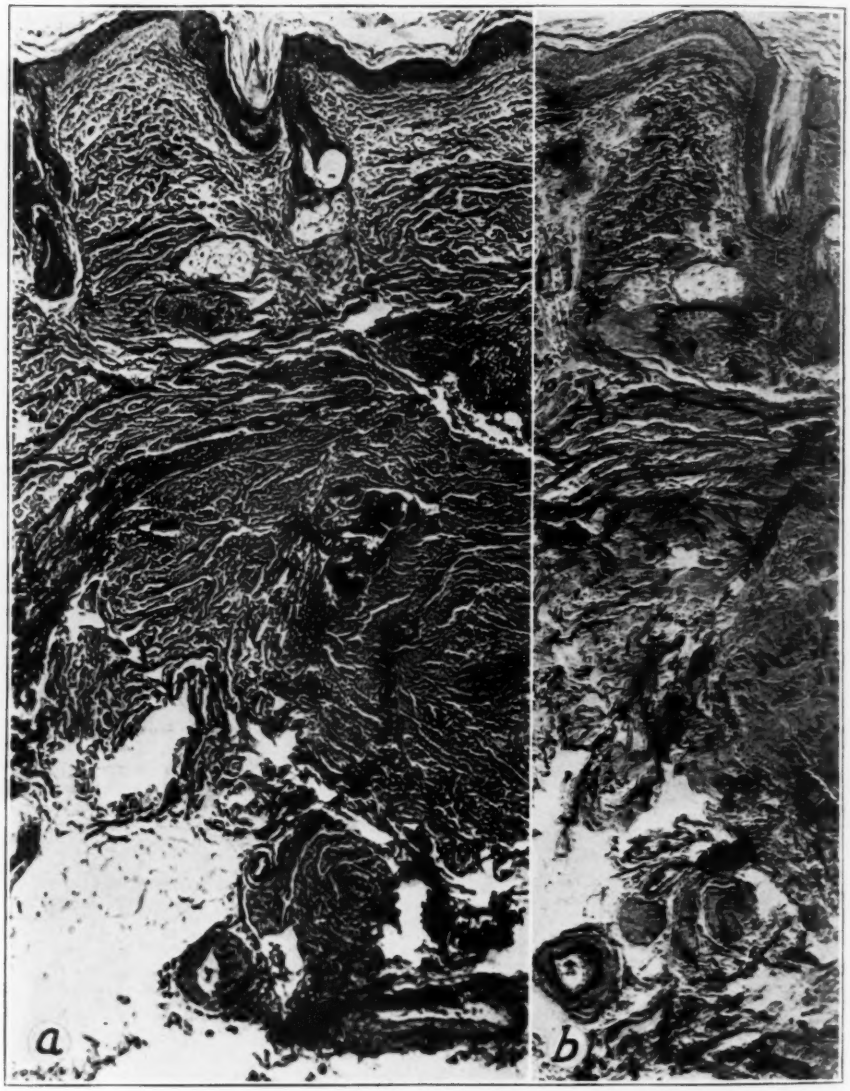

Fig. 5.—Skin taken from the dorsum of the hand in a case of acrosclerosis of five years' duration. Important changes shown (*a*) are atrophy of the hair follicles and sebaceous glands, homogenization of collagen and thickening of the walls of the blood vessels (hematoxylin and eosin, × 60). The tissue in *b* is stained with elastin H to illustrate the proliferation of the intima and the swelling and fragmentation of the elastic fibers (× 60).

identical with those involved by acrosclerosis, but altogether the disease suggests a persistent edematous or infiltrative stage of generalized progressive scleroderma limited to the acral parts and the absence of primary vasomotor abnormalities precludes any possibility of confusion with acrosclerosis.

HISTOLOGIC CHARACTERISTICS OF ACROSCLEROSIS

Study of specimens of skin taken from the dorsal aspects of the hands and fingers indicates that the changes in acrosclerosis are the same as those of diffuse scleroderma. The salient changes appear in the cutis (fig. 5), especially in the lower two thirds, where the collagen appears in compact, homogeneous, relatively acellular coarse bundles. Elastic fibers are usually fragmented and are sometimes swollen and decreased in quantity. The cutis may be of diminished thickness. Important changes constantly occur in the blood vessels, the endothelial cells of which are swollen or proliferated and the walls greatly thickened, the resulting encroachment on the lumen leading at times to occlusion. Thromboses were not observed in our material, although they undoubtedly occur.[16]

The epidermis may show hyperkeratosis, and the rete may be acanthotic or atrophic. Increased deposits of melanin pigment accumulate in the basal cells. Hair follicles and sebaceous glands are wasted or absent, and arrectores pilorum muscles occur independently of hair follicles. The sweat glands usually remain well preserved, in some sections appearing abnormally close to the surface of the skin owing to atrophy of the cutis.

Microscopic examination of skeletal muscles in a few cases disclosed interstitial inflammation, obliterative changes in the blood vessels and homogenization of the muscle bundles.

TREATMENT

In favorable cases treatment of acrosclerosis may result in a material remission of sclerosis by inducing relaxation of arterial spasm. The clothing must be adequate, and exposure to inclement weather and great changes in weather should be discouraged; residence should be preferably in a hot, dry climate. Protection of the fingers from trauma (including immersion in cold water) is important, as is also their treatment daily with a bland emollient. Tobacco is interdicted. To spare the patient emotional and psychic stresses, social, domestic and economic readjustments must be made.

16. Lewis, T.: The Pathological Changes in the Arteries Supplying the Fingers in Warm-Handed People and in Cases of So-Called Raynaud's Disease, Clin. Sc. **3**:287-319 (Aug. 15) 1938.

Intravenous injections of foreign protein, usually typhoid vaccine, have resulted in improvement in some cases by releasing the peripheral vasomotor tone. Daily injections of solution of posterior pituitary over a long period, as recommended by Oliver and Lerman,[17] are of slight benefit. In theory such a potent vasoconstrictor would seem to be objectionable, but we have not observed any ill effects. Mecholyl chloride (acetylbetamethylcholine chloride), administered orally, by hypodermic injection or by iontophoresis, has been tried, although the results have not been outstanding as far as we can determine. Prostigmine [18] may be of value, given orally as the bromide or subcutaneously as the methylsulfate. Physical therapy, consisting particularly of heat and massage, will aid in maintaining the dermal nutrition. With the use of insulin-free extracts of pancreas or of other tissue extracts we have not seen any impressive effects.

Sympathectomy [19] has unfortunately not yielded the substantial proportion of favorable results in acrosclerosis that it has in Raynaud's disease. Operation, if performed at all, should be restricted to cases in which there are mild sclerosis and high vasomotor index [20]—cases, in other words, in which there are slight sclerodermic changes and pronounced manifestations of Raynaud's disease. It must, of course, be recognized that the interruption of the vasomotor pathways may not cause appreciable retrogression of obliterative changes in the vascular system or of strangling fibrosis in the skin and that ischemic phenomena will therefore persist. When lumbar sympathectomy is performed, however, the results seem to be entirely successful in relieving symptoms in the lower extremities.

In recent years parathyroidectomy [21] has been credited with favorable results in these cases, but not unanimously.[22] We have not had any experience with it, nor have we had any with the use of dihydrotachysterol.[23]

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17. Oliver, E. L., and Lerman, J.: Scleroderma Treated with Injections of Posterior Pituitary Extract, Arch. Dermat. & Syph. **34**:469-477 (Sept.) 1936.

18. Perlow, S.: Prostigmine in the Treatment of Peripheral Circulatory Disturbances, J. A. M. A. **114**:1991-1993 (May 18) 1940.

19. Smithwick, R. H.: The Rationale and Technic of Sympathectomy for the Relief of Vascular Spasm of the Extremities, New England J. Med. **222**:699-703 (April 25) 1940.

20. Adson, A. W.; O'Leary, P. A., and Brown, G. E.: Surgical Treatment of Vasospastic Types of Scleroderma by Resection of Sympathetic Ganglia and Trunks. Ann. Int. Med. **4**:555-568 (Dec.) 1930.

21. Bernheim, A. R., and Garoloch, J. H.: Parathyroidectomy for Raynaud's Disease and Scleroderma: Late Results, Arch. Surg. **38**:543-555 (March) 1939.

22. Liuzzo, G.: La paratiroidectomia nella sclerodermia, Policlinico (sez. prat.) **47**:41-50 (Jan. 15) 1940.

23. Hummel, B.: Erfahrungen über den Heilfaktor A T 10 bei der Sklerodermie, München. med. Wchnschr. **1**:96-98 (Jan. 20) 1939.

COMMENT

Several noteworthy investigations on the interrelation of pathologic arterial spasm and scleroderma are recorded in the literature. However, it is still uncertain whether the vasomotor disturbance underlying acrosclerosis and that underlying Raynaud's disease are identical. Lewis and Kerr [24] segregated cases of Raynaud's syndrome in which sclerodermic changes developed from cases of the uncomplicated variety of Raynaud's disease, stating:

> It is quite possible that patients who in the first instance display attacks of cyanotic fingers and subsequently acquire a general scleroderma are of essentially the same type [as those who have the classic form of Raynaud's disease]; but as we have not as yet proof that the vessels in these cases respond directly and unusually to temperature, and as we do not understand how the general sclerosis of the skin occurs, it is quite clearly desirable that this class of cases should be kept apart until it has been submitted to suitable investigation.

In support of the isolation of these two types of the disease Lewis and Pickering [25] added further the arguments that, first, the development of sclerodactylia from digital arterial spasm is by no means invariable and, second, in cases of facial scleroderma local arterial spasm has yet to be demonstrated.

Lewis and Landis [26] attributed the acral distribution of scleroderma in such cases to the fact that the parts of the skin involved are those which are much exposed to the air and which therefore become cold most readily. Their hypothesis is that circulatory disturbances underlying the scleroderma arise from a local fault in the vessels themselves rather than in the nervous system. Secondarily, structural changes occur which contribute to the circulatory troubles by reenforcing the spasmodic obstruction.

An enlightening study on the mechanism of the circulatory insufficiency in the vasomotor form of sclerodactylia was contributed by Prinzmetal.[12] Impressed by the observation that the development of sclerodactylia in a case of Raynaud's disease results in inability to maintain normal cutaneous temperature, this investigator applied tight rubber finger cots to normal subjects and showed that the same temperature reactions occurred on the constricted parts as in sclerodactylia. This demonstration, which is supported by studies of the cutaneous

24. Lewis, T., and Kerr, W. J.: Experiments Relating to the Peripheral Mechanism Involved in Spasmodic Arrest of the Circulation in the Fingers: A Variety of Raynaud's Disease, Heart **15**:7-101 (Aug.) 1929.

25. Lewis, T., and Pickering, G. W.: Observations upon Maladies in Which the Blood Supply to Digits Ceases Intermittently or Permanently, and upon Bilateral Gangrene of Digits; Observations Relevant to So-Called "Raynaud's Disease," Clin. Sc. **1**:327-366 (Dec.) 1934.

26. Lewis, T., and Landis, E. M.: Further Observations upon a Variety of Raynaud's Disease, with Special Reference to Arteriolar Defects and to Scleroderma, Heart **15**:329-350 (July 27) 1931.

capillaries,[27] confirmed the suggestion of Mayo and Adson [28] that hypertrophy of the collagen intensifies the ischemia in these cases by compressing and strangulating the blood vessels.

In some cases of Raynaud's disease morphologic changes have not been demonstrated,[29] whereas in others alterations have been described in the vascular system or the nervous system or both, with incrimination particularly of the smaller arterioles and the finer ramifications of nerves.[30] But pathologic anatomy has not provided an adequate explanation for the intermittent arteriolar spasm first suggested by Raynaud—the hypothesis that the disease which he described is purely a vasomotor disturbance at present has more evidence to support it than any of the alternative possibilities. Some writers consider the vascular sclerosis a result of vasoconstriction, the organic changes contributing further to the increased duration of attacks and trophic complications in a vicious cycle. Lewis's recent observations,[16] however, do not support the concept that attacks of spasm alone in Raynaud's disease lead to thickening of the digital arteries.

Certain aspects of acrosclerosis indicate clearly a close relation to Raynaud's disease: [31] the fact that it occurs chiefly among women, the absence of the condition in childhood, the character of the vasomotor events and the precipitation of paroxysms by cold or emotional stress. The intimate connections with Raynaud's syndrome were clearly perceived by Hutchinson. Supervention of sclerosis over the distal phalanges in Raynaud's syndrome is a fairly common complication, occurring in 10 per cent of cases, and this may develop early or late in the course of the disease. We have arrived at the view that, although the mechanism is obscure, acrosclerosis is a form of the Raynaud syndrome in which a variety of trophic disturbances have localized on the hands and face concomitantly with or consecutively to the vasomotor changes. We believe that the name acrosclerosis may be properly applied to the instances of sclerodactylia which occur in Raynaud's disease, even though

27. Brown, G. E.; O'Leary, P. A., and Adson, A. W.: Diagnostic and Physiologic Studies in Certain Forms of Scleroderma, Ann. Int. Med. **4**:531-554 (Dec.) 1930.

28. Mayo, W. J., and Adson, A. W.: Raynaud's Disease, Thrombo-Angiitis Obliterans and Scleroderma: Selection of Cases for and Results of Sympathetic Ganglionectomy and Trunk Resection, Ann. Surg. **96**:771-783 (Oct.) 1932.

29. Craig, W. M., and Kernohan, J. W.: The Surgical Removal and Histological Studies of Sympathetic Ganglia in Raynaud's Disease, Thrombo-Angiitis Obliterans, Chronic Infectious Arthritis, and Scleroderma, Surg., Gynec. & Obst. **56**:767-778 (April) 1933.

30. Sunder-Plassmann, P.: Die Raynaudsche Erkrankung und ihr Formenkreis, Deutsche Ztschr. f. Chir. **251**:125-194, 1939. Sunder-Plassmann, P., and Jaeger, F.: Raynaud + Sklerodermie, ibid. **253**:263-292, 1940.

31. Allen, E. V., and Brown, G. E.: Raynaud's Disease: A Clinical Study of One Hundred and Forty-Seven Cases, J. A. M. A. **99**:1472-1477 (Oct. 29) 1932.

facial involvement is absent. Hunt,[32] in his statement that scleroderma involves the face in three fourths of the cases, has implied a concept of acrosclerosis which is similar to ours.

We propose that the name acrosclerosis be reserved for the condition in which vasospastic phenomena appear early and are usually outstanding. There is a possibility that acrosclerosis is only a complicated form of Raynaud's "disease," but for the present we prefer to classify it apart. We view its relation to diffuse progressive scleroderma as a distant one, and we have indicated the morphologic and topographic distinctions from this type of scleroderma. We must emphasize that all of the foregoing entails more than an academic question of terminology for varying degrees of the same condition. So long as the biologic distinctions underlying these three states (Raynaud's disease, acrosclerosis and diffuse scleroderma) remain unknown, we believe that the distinguishing terminology must be retained. And so long as different diagnostic and prognostic essentials are implied by each of these names, the nomenclature is not unduly overburdened.

SUMMARY

The vasomotor types of sclerodactylia and diffuse scleroderma have been reviewed in order that their characteristics and relation may be more clearly defined. The morphologic features of acrosclerosis have been desecribed, and the suggestion is offered that the concept of acrosclerosis be enlarged by including also those examples of Raynaud's "disease" which present sclerotic complications in the skin of the fingers and hands. Prognosis with regard to life and to improvement is favorable for acrosclerosis as compared with the prognosis of diffuse scleroderma. Ordinarily acrosclerosis attains a certain intensity and distribution, after which the disease remains stationary without further extension. Instances of substantial involution have been observed, occurring spontaneously and after surgical and nonsurgical treatment. In diffuse scleroderma the benign features of acrosclerosis are replaced by characteristics which predicate a serious outlook. We have shown that if after two years the sclerosing process has not extended beyond the acral parts, it is unlikely that generalization will subsequently take place.

We agree with Lewis and others that, provisionally, the complicated and the uncomplicated form of Raynaud's syndrome should be regarded as distinct. However, one is unable to detect differences in the vasospastic manifestations of ordinary Raynaud's disease and the prodromal symptoms of acrosclerosis and of progressive scleroderma. The pertinent literature has been surveyed and hypotheses of pathogenesis are presented, but we are obligated to conclude that the relation between arterial obstruction and scleroderma is only incompletely understood.

32. Hunt, J. H.: The Raynaud Phenomena: A Critical Review, Quart. J. Med. **5**:399-444 (July) 1936.

KERATOSIS FOLLICULARIS WITH UNUSUAL INVOLVEMENT OF THE SCALP

REPORT OF A CASE

DAVID G. WELTON, M.D.
CHARLOTTE, N. C.

Extensive alopecia is not a common clinical manifestation of keratosis follicularis. Most of the clinical reports and textbook descriptions, including Darier's own,[1] mention involvement of the scalp as being similar to the crusting forms of seborrhea, sometimes with scaly papules but with no tendency to loss of hair. A patient with extensive lesions of the scalp associated with almost total alopecia and obliteration of most of the finger and toe nails, in addition to characteristic lesions of the skin, has been under my observation for over three years. Since this combination of abnormalities appears to be rare in keratosis follicularis, it is felt that the following report should be added to the literature.

REPORT OF CASE

History.—F. C., a white woman aged 29, single, was first seen in January 1939. Since childhood she had had a generalized thickening and spiny roughness of the skin with such severe involvement of the palms and soles that deformities had resulted. The hair of the scalp and body had always been lacking until six years previously, when a sparse growth appeared in the axillas and a few hairs were noted around the sides of the scalp. She had worn a wig for many years. The eruption on the hands and feet involved the nail bed to such an extent that only two or three partial nails had been present for years. In 1933 and in 1935 the patient had been treated by superficial roentgen irradiation by another physician and had experienced temporary relief of symptoms. She was subject to frequent "spells" of nervousness and found it difficult to adjust herself to society. All the teeth had been extracted many years before because of abscesses. She gave no history of having taken arsenic in any form. Her other past history and her family history were noncontributory.

Examination.—The patient appeared older than her stated age. The scalp was the site of numerous greasy, horny, papulofollicular lesions, many of which were aggregated into clusters forming plaques. Others were scattered diffusely, giving a "stippled" sensation on palpation. A few relatively smooth areas were present. The hair was almost entirely lacking, a few short hairs being present near the ears. The skin of the face was thick and showed deep rhagades around the mouth. The eyebrows were almost entirely lacking. Both jaws were edentulous, but no lesions were found on the mucous membranes. The skin of the trunk and extrem-

1. Darier, J.: A Textbook on Dermatology, Philadelphia, Lea & Febiger, 1920, p. 231.

ities exhibited in symmetric fashion characteristic, slightly greasy, firm, follicular papules, light tan to brown and so widespread that virtually not 1 square inch of normal skin could be found. There were no hairs on the body, except a few in the axillas. On the dorsa of the hands there were several small pea-sized verrucous lesions somewhat suggestive of arsenical keratoses (microscopic examination of one showed that it was not malignant). The most severe involvement was seen in the palms and soles. The palms were studded with beefy red hyperkera-

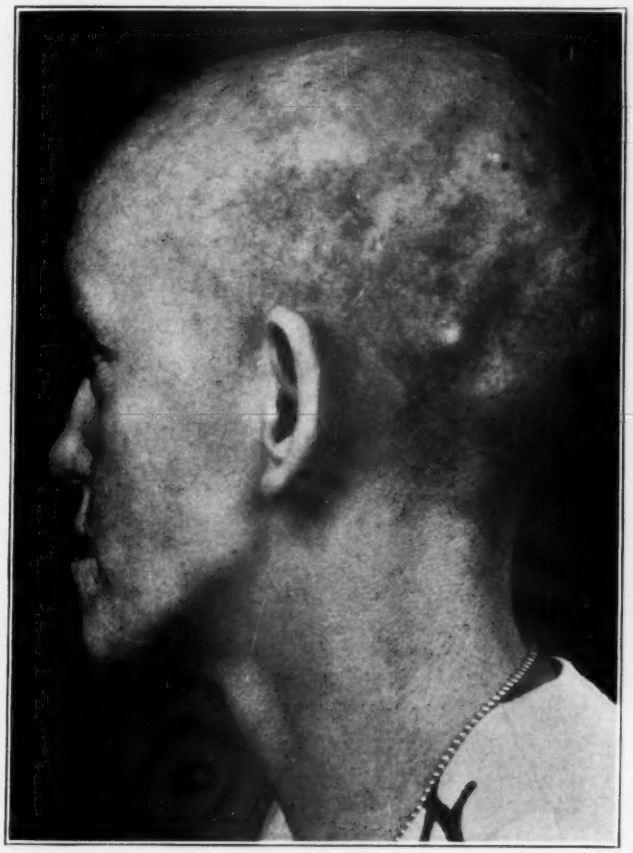


Fig. 1.—Darier's disease associated with almost total alopecia of the scalp.

totic lesions which were thick and interlaced with atrophic, white areas. The patient was unable to flex the fingers more than a few degrees except with difficulty. The soles were covered with filiform, hyperkeratotic lesions over 1 cm. thick and palisaded together to form a stiff, horny pad. The finger and toe nails were almost wholly obliterated. No vesicles were found. On the inner aspect of the left foot, just below the ankle bone, there was a deep ulcer with a dirty, purulent discharge and a foul odor. A similar lesion subsequently developed in the corresponding area on the other foot.

Laboratory Data.—The Wassermann, Kahn and Kline reactions of the blood were negative. Examination of the blood showed 4,370,000 red cells, 13.6 Gm. of hemoglobin and 14,350 white cells, with 70 per cent polymorphonuclear leuko-

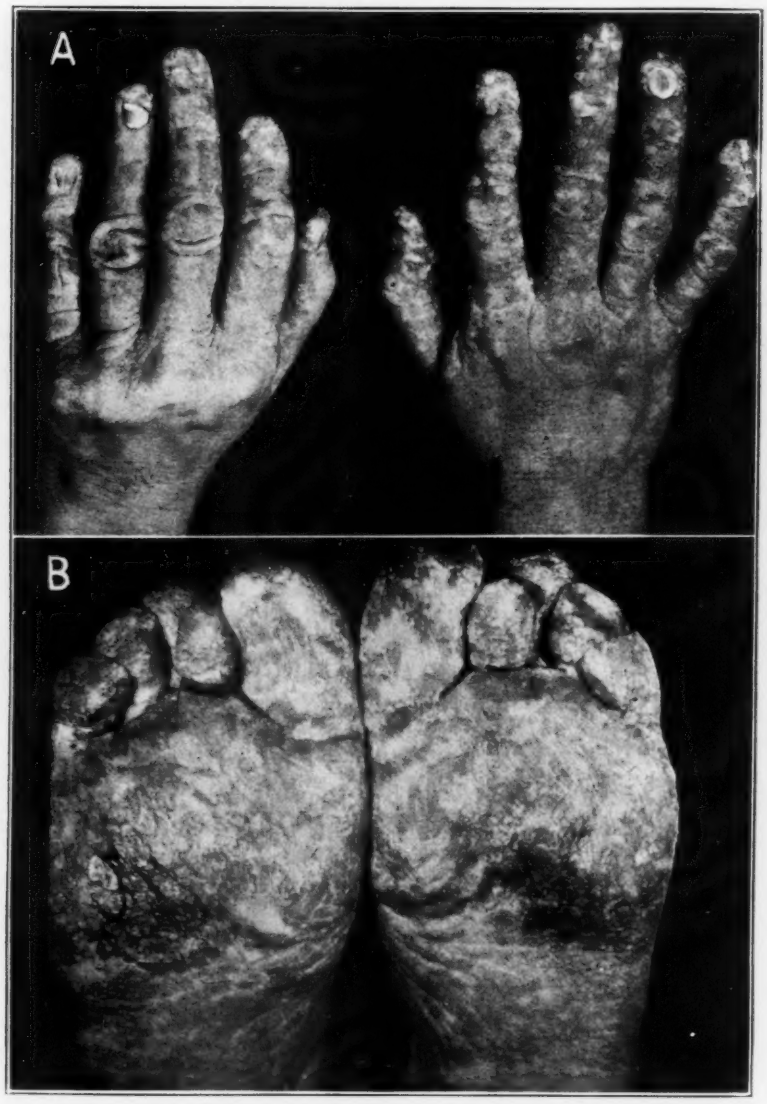


Fig. 2.—Patient with keratosis follicularis, showing (*A*) cutaneous involvement and loss of several nails and (*B*) diffuse hyperkeratosis of the soles.

cytes, 26 per cent lymphocytes and 4 per cent mononuclear leukocytes. The urine was normal. The basal metabolic rate was + 17 per cent. The blood cholesterol was 138 mg. per hundred cubic centimeters.

Histologic Study.—Specimens for biopsy were taken from five different areas and showed the microscopic characteristics of keratosis follicularis (hyperkeratosis, numerous horny plugs, *corps ronds,* grains, irregular acanthosis and little inflammatory infiltrate in the corium in most sections). The most interesting specimen was that from the scalp, taken at the suggestion of Dr. Lee McCarthy,[2] who studied the sections and made the following report: "I feel that there are enough points of pathologic change characteristic of Darier's disease to make a diagnosis. *Corps ronds,* if carefully looked for, can be found in the epidermis, which is atrophic from pressure of horny material. Many grains can be seen in the loosely laminated, horny mass. Space formation is scarce but can be seen if looked for in several places. The invaginations and hyperkeratosis are self evident and even greatly exaggerated. In the cutis there is ample evidence of abortive hair proliferation with practically total loss of hair of the terminal type. In some

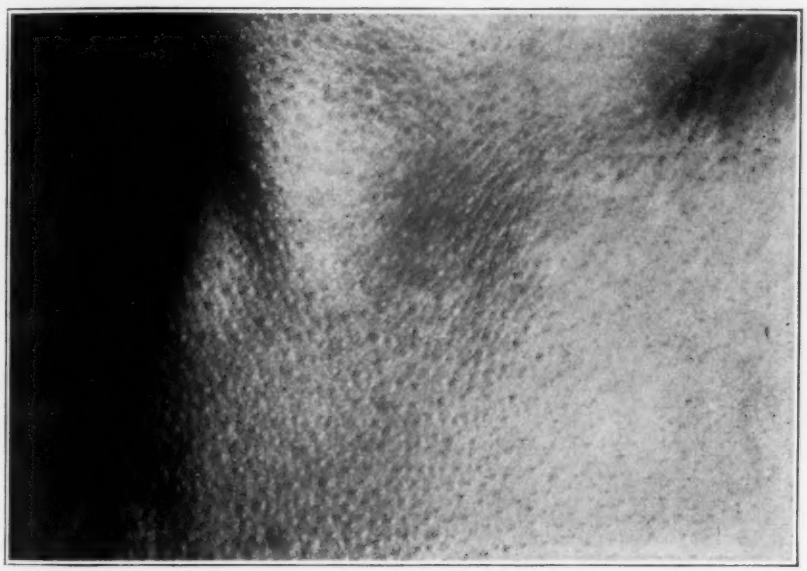


Fig. 3.—Follicular keratosis at the base of the neck.

of these abortive hair walls I thought I could see signs of this disease. There is also a cystic degeneration of the sebaceous glands." The sections from the scalp were also submitted to Dr. U. J. Wile, who agreed with the diagnosis.

Treatment and Subsequent Course.—Since the patient had already been given considerable roentgen therapy, further irradiation was deemed inadvisable. Intravenous injections of gold sodium thiosulfate (maximum dose 25 mg.) were given weekly for three months; some symptomatic improvement was noted at first, but the injections were discontinued because of definite increased pruritus following the last two. In addition, 40 per cent salicylic acid plasters and ointments were used on the palms and soles and softening creams on the body. Recurring fissures of the lips were touched with 10 per cent silver nitrate. Riboflavin by mouth did not influence these lesions.

2. McCarthy, L.: Personal communication to the author.

The patient was presented at the meeting of the Baltimore-Washington Dermatological Society, held at Duke Hospital, Durham, N. C., in October 1939.[3] All the members agreed with the diagnosis. Suggestions for therapy included high doses of vitamin D. The patient was given 50,000 U. S. P. units of vitamin D daily in the form of drisdol (crystalline vitamin D_2 [calciferol]) in propylene glycol. After three weeks some symptomatic improvement was reported, but no change in the lesions could be detected. The administration of vitamin D was continued for eight months, and the patient's symptoms later became much worse while taking it. Irradiation of the palms and soles with a quartz mercury vapor glow lamp was tried, without benefit.

In March 1941, after the publication of Peck, Chargin and Sobotka,[4] the patient was given high concentrations of vitamin A, 100,000 U. S. P. units daily

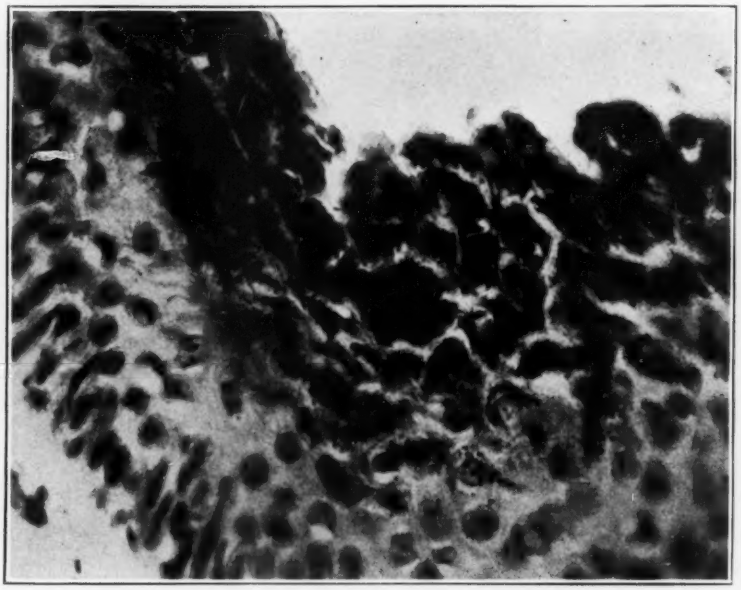


Fig. 4.—Photomicrograph (lesion of the scalp) showing dyskeratotic cells (high power).

by mouth. Within three weeks she reported symptomatic improvement; in six weeks she noted that the skin of the body felt softer, but the palms and soles were unaffected. The dose was then lowered to 80,000 U. S. P. units daily for the next six months, and no further improvement occurred. In October 1941, after taking no vitamin A for six weeks, the patient was given a different brand and a much larger dose: 300,000 U. S. P. units daily. Two weeks later she reported the first symptomatic improvement of the hands, and a sample of blood was taken for vitamin A determination. The examinations of the blood were

3. Elliott, J. A., and Welton, D. G.: Keratosis Follicularis, Arch. Dermat. & Syph. **42**:354 (Aug.) 1940.

4. Peck, S. A.; Chargin, L., and Sobotka, H.: Keratosis Follicularis, Arch. Dermat. & Syph. **43**:223 (Feb.) 1941.

made at the Duke Laboratory through the cooperation of Dr. J. L. Calloway, and the results are shown in the accompanying table. This first reading showed a vitamin A level higher than normal. The dose was then reduced to 150,000 U. S. P. units daily for ten weeks, with no further subjective change. Up to this point I was still skeptical about any actual benefit from the vitamin A. In an effort to determine whether the effect was merely psychic, the administration of all vitamins was stopped for eight weeks. At the end of this period a blood determination showed findings below normal (on table, February 3). Placebo capsules identical in appearance with the capsules of vitamin A were then administered for two weeks, after which the patient reported that she felt worse. When she was again given 200,000 U. S. P. units daily of vitamin A she soon "felt like a different person," and her skin became softer and more pliable objectively as well as subjectively. The face became smoother, and the scalp felt better. After four weeks the blood level of vitamin A rose to normal. No change in the amount of hair has been noted.

Determinations of Carotene and Vitamin A in the Blood*

Date	Plasma Carotene (Normal, 150 to 500)	Vitamin A (Normal, 70 to 200)
November 3	287	243
February 3	177	98
March 5	212	149

* All figures represent U. S. P. units per hundred cubic centimeters of blood.

COMMENT

Lesions of the scalp have been mentioned in many other reports of keratosis follicularis, but extensive involvement of the scalp associated with almost total alopecia, apparently as a result of involvement of the hair follicles by the same pathologic process, is rare. In 1 of Bowen's cases [5] there was a "scalp covered with a thick mass of greasy concretions, closely aggregated, removal of which revealed that they dipped down into shallow crateriform depressions surrounded by a slightly elevated rim." Lesser [6] described the case of a boy aged 6 years whose scalp showed only a few isolated hairs centrally and a scanty growth peripherally, with epidermal spines projecting from a number of follicles and eyebrows entirely wanting. Biopsy of the scalp was not performed.

The combination of alopecia and changes in the nails in addition to the classic lesions of the skin in the case reported might be interpreted as a manifestation of a congenital ectodermal defect or dysplasia. The administration of vitamin A in high doses has been more successful

5. Bowen, J. T.: Keratosis Follicularis, Apropos of a New Case, J. Cutan. & Genito-Urin. Dis. **14**:209 (June) 1896.

6. Lesser: Diseases of the Skin, cited by Morrow, P. A.: Keratosis Follicularis, Associated with Fissuring of the Tongue and Leukoplakia Buccalis, J. Cutan. & Ven. Dis. **4**:257 (Sept.) 1886.

than any other new therapeutic measure reported in recent years. Peck, Chargin and Sobotka reported actual involution of lesions. Although my patient experienced chiefly symptomatic relief, there was definite softening and increased pliability of the skin, which is all that reasonably could be expected in view of such advanced lesions. This patient continues to feel comfortable as long as she maintains a dose of 200,000 U. S. P. units of vitamin A daily. In this circumstance, Peck, Chargin and Sobotka stated the belief that there is an inherent inability to convert the provitamin into vitamin A.

SUMMARY

A case of keratosis follicularis with extensive lesions of the scalp and almost total alopecia, in addition to far advanced, characteristic lesions of the skin and nail beds is reported. Definite symptomatic improvement was obtained by the oral administration of high doses of vitamin A.

Suite 718, Professional Building.

Clinical Notes

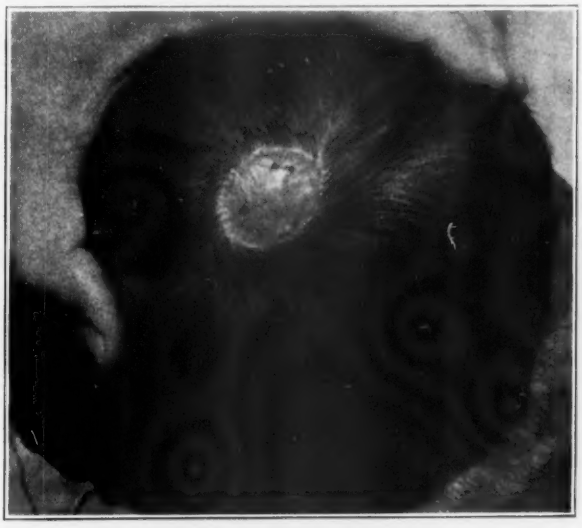
CONGENITAL DEFECT OF THE SCALP

ROBERTO QUERO, M.D., HABANA, CUBA

Anderson and Novy [1] recently recorded 4 cases of a peculiar congenital defect of the scalp, thus publishing the second article on this subject in the American literature. As these authors consider that this defect is not familiar to the majority of dermatologists, it might be of interest to add a sixth case of my own.

REPORT OF A CASE

A. R., a 5 year old white Cuban girl, came to the dermatologic consultation of the Hospital Municipal de Infancia de la Habana, on April 19, 1940. She



Congenital defect of the scalp.

was brought by her parents for treatment of a patch of alopecia which she had had on the vertex since birth.

She presented on the vertex a round bald scleroderma-like plaque, 3 cm. in diameter, ivory white, smooth, polished and shiny. On palpation, this plaque was adherent to the underlying aponeurosis and somewhat depressed below the surface. On this area it was impossible to detect even with the aid of a magnifying glass the slightest trace of lanugo hairs or hair follicles. The sensations were normal, and injections of histamine phosphate and pilocarpine hydrochloride

From the Consultation of Skin Diseases and Syphilis at the Hospital Municipal de Infancia de la Habana.

1. Anderson, N. P., and Novy, F. G.: Congenital Defect of the Scalp, Arch. Dermat. & Syph. **46**:257 (Aug.) 1942.

did not show any abnormality of the vegetative nervous system. Three punctate hemorrhagic crusts were present on the central portion of the plaque and another near the edge. When they were removed, the underlying scalp appeared slightly depressed and whiter than the rest of the plaque. The parents stated that these lesions were produced by the comb and that the girl always refused to have her hair dressed. The rest of the scalp, the eyebrows and the eyelashes were normal. The rest of the integuments, the finger nails of both hands and feet, the teeth and the sweat organs were also normal.

The history the parents gave was as follows: They first noticed the defect almost immediately after birth, there being a complete lack of lanugo on this area. The obstetrician could not offer any explanation of the defect, as the delivery was normal. At the child's birth the plaque was about 2 cm. in diameter, but it enlarged until she was 4 years old and has since remained stationary. She had never complained of itching, pain or other abnormal sensations.

The Kahn reaction of the blood was negative. The basal metabolic rate was +5 per cent. The calcium content of the blood was 11 mg. per hundred cubic centimeters and the phosphorus content 3.5 mg. When the girl was referred to the medical service for general examination, it was reported that she was normal. The roentgenogram of the skull showed no abnormality. Permission for biopsy was refused.

The parents were in good health, and the Kahn reaction of the blood of both was negative. No similar disease had even been noted in any other member of the family. There were three normal brothers and sisters, two of them older and one younger than the patient.

From the clinical viewpoint, the skin of the surface of the plaque had the appearance of morphea, though the congenital character, the localization on the vertex and the round form made the diagnosis of congenital defect unmistakable. This round scleroderma-like congenital defect of the scalp is the only one on record among 85,402 cases observed in the hospital from 1935 to date.

MEDIAN CANAL-LIKE DYSTROPHY OF THE NAIL

Report of a Case

OSWALDO G. COSTA, M.D., BELLO HORIZONTE, BRAZIL

A peculiar dystrophy of the nails was first described in 1928 by Heller [1] under the title "Dystrophia Unguium Mediana Canaliformis." Other cases were later reported by Wucherpfeinning,[2] Ledo,[3] Pardo-Castello [4] and Gottron.[5] As my case is apparently the first to be recorded in Brazil, it seemed worthy of publication.

From the Clinic of Syphilis and Cutaneous Diseases, University of Minas Geraes.

1. Heller, J.: Dermat. Ztschr. **51**:416-419 (Jan.) 1928.
2. Wucherpfeinning, V.: Dermat. Ztschr. **54**:96-98 (Aug.) 1928.
3. Ledo, E.: Ann. de dermat. et syph. **10**:765-767 (July) 1929.
4. Pardo-Castello, V.: Diseases of the Nails, ed. 2, Baltimore, Charles C Thomas, Publisher, 1941, p. 96.
5. Gottron, in Nekam, L.: Corpus iconum morborum cutaneorum, Leipzig, Johann Ambrosius Barth, 1939, pt. 3, p. 820.

REPORT OF CASE

C. N. G., a Negro aged 25, a soldier, was born and resided in Bello Horizonte. The family and personal history were irrelevant, and no disease of the nails had affected any member of his family.

The disease for which the patient sought medical advice affected the nail of the left ring finger and had been present continuously for ten years. The abnormality consisted of a longitudinal furrow or canal which affected the central part of the nail and extended from the root to the free border. It measured 8 mm. in length. At the site of the furrow the nail was thin and covered with a slight lamellar desquamation. The nail was normal in other respects, there being no paronychia or dermatitis of the surrounding parts. There were no subjective symptoms, and there was no history of previous injury to the nail. Microscopic and cultural examination of the nail showed no mold. The Wassermann and

Median canal-like dystrophy of the nail.

Kahn reactions of the blood were negative, and a general physical examination, including examination of the hair and teeth, showed no abnormalities. Treatment by roentgen rays was unsuccessful.

COMMENT

The cause of this disease is unknown. Heller, cited by Pardo-Castello, considered it a dystrophy, probably of nervous origin, affecting the normal keratinization of the nail at a certain part of the matrix. In differential diagnosis, I excluded the possibility of onychorrhexis as described by Dubreuilh.[6]

Rua Ceará 1695.

6. Dubreuilh, W., in Besnier, E., and others: La pratique dermatologique, Paris, Masson & Cie, 1902, pt. 3, p. 619.

Correspondence

SARCOID AND TUBERCULOSIS

To the Editor:—I should like to call attention to an important exception to Dr Ronchese's conclusion (ARCH. DERMAT. & SYPH. **46**:860 [Dec.] 1942) that "sarcoid and sarcoidosis are attenuated forms of tuberculosis." This statement is reminiscent of the "not even yet dead belief," particularly among specialists in tuberculosis, that erythema nodosum is always, or nearly always, due to tuberculosis.

The exception to which I refer is sarcoid (of the skin or of the peripheral nerves) due to leprosy. It is usually referred to by leprologists as "tuberculoid leprosy" or as "the tuberculoid form of neural leprosy," as opposed to nodular, or lepromatous, leprosy. It is characterized by: (1) sarcoid-like cutaneous plaques, which are sometimes annular; (2) anesthesia, always to heat and cold and frequently to light touch as well, either in the lesions or elsewhere; (3) thickening of peripheral nerve trunks (not always present), often in the vicinity of the lesion (or lesions); (4) negative "snips" on examination for Mycobacterium leprae, and (5) the usual histologic features of sarcoid—relatively discrete multiple epithelioid cell tubercles with occasional giant cells, little or no central necrosis, few lymphocytes and few or no acid-fast bacilli; unusual involvement of the vessels or damage to nerves may be seen and when present suggests that the lesion is leprosy.

So far as I am aware, in no case has sarcoidosis—true Besnier-Boeck-Schaumann disease, with disseminated lesions in the skin, lungs, uvea and bones or any combination of these—ever been shown to be due to leprosy.

The prognosis in tuberculoid leprosy is in general good; spontaneous involution of the lesions in from one to three years is to be expected without any specific treatment, and relapse is unlikely, though progression of neural lesions may occur. Rarely, tuberculoid leprosy may turn out to be nodular (lepromatous leprosy in a bacteriologically negative phase; in this event acid-fast organisms will become apparent in the lesions and clinical progression, often in the form of a series of acute relapses, will occur. This is an unusual circumstance, however, particularly when the original diagnosis of tuberculoid leprosy is well founded.

It should be routine clinical practice to examine all patients with sarcoid of the skin with the utmost care for both thermal anesthesia and thickening of peripheral nerve trunks, especially the ulnar and the greater auricular. The 6 patients with sarcoid I have observed in my own practice in Honolulu in the past three years have all turned out to have tuberculoid leprosy.

HARRY L. ARNOLD JR., M.D., Honolulu, Territory of Hawaii.

Obituaries

FRANK W. CREGOR, M.D.

1873-1942

Dr. Frank W. Cregor died on Dec. 9, 1942, at the age of 69 years, of prolonged cardiovascular illness. He was born on July 13, 1873, of farmer parents, Althedore and Martha Caroline Peed Cregor, in Henry County, Ind., near the city of Newcastle.

Dr. Cregor was graduated in 1894 from the Indianapolis Medical College, which was one of the schools that later combined to form Indiana University School of Medicine. For a number of years following his graduation Dr. Cregor was engaged in country practice, first in the town of Carthage and later in the larger town of Greenfield, Ind.

In 1911 he became interested in dermatology, and after working for a time in dermatologic clinics in the city of New York he went to the University of Vienna to continue his graduate study. In 1912 he returned to Indianapolis, where he practiced dermatology until a few months before his death. On his return to the United States, he was befriended by the pioneer dermatosyphilologist of this section, Dr. Alembert Brayton, who was professor of dermatology in the newly organized Indiana University School of Medicine. On the retirement of Dr. Brayton, Dr. Cregor became professor and taught in the classrooms of that school and the outpatient departments of Robert W. Long Hospital, William Coleman Hospital, James Whitcomb Riley Hospital for Children and Indianapolis City Hospital. His tenure of this position was long and was terminated by illness, which forced his retirement about one year ago. To him can be accredited in general the present knowledge of dermatology of the general practitioners and several specialists in this field who are practicing in the state of Indiana.

Dr. Cregor was greatly interested in civic as well as in professional matters. He served his state as senator in the Indiana General Assembly of 1899 and 1901. In 1932 he was a member of the Indiana State Board of Health. In 1912 Dr. Cregor became a member of the Indianapolis Medical Society, and he belonged to this group at his death. Over a period of twenty-five years he was active in the Indiana State Medical Association, serving as a member of the legislative and public policy committees and in various other capacities. In 1927 he became president of the Indiana State Medical Association. Dr. Cregor served the American Medical Association for ten years as a member of the Judicial Council. He was elected a member of the American Dermatological Association in 1929 but resigned a few years ago.

Dr. Cregor possessed a keen knowledge of the land and of people. He had an abiding interest in farming and at the time of his death was successfully operating several tracts. He had a keen business judgment, which brought him and his family financial comfort. His list of professional publications was not lengthy, but some of them were basic.

FRANK W. CREGOR, M.D.
1873-1942

Dr. Cregor was twice married. His first wife and a son by that union died many years ago. In 1913 he married Miss Margaret Gertrude Horn of Valparaiso, Ind., and from that union was born a daughter, Mrs. Mary Cregor Manouge, of Indianapolis, and a son, John, now serving in the United States Navy.

JOHN ERIC DALTON, M.D.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

COMMERCIAL ENDOCRINE PREPARATIONS. ELMER L. SEVRINGHAUS, Endocrinology **30**:912 (June) 1942.

Sevringhaus presents a clear concise summary of the current status of the various endocrine preparations with particular reference to the cost and mode of administration. It would seem worth while to repeat here a few of the points made by this authority.

Thyroid.—The standard preparation of thyroid has been for many years the desiccated gland substance whose potency is specified in terms of its content of iodine, 0.2 per cent. There exist in the United States three other competing types of thyroid tablets: (*a*) some standardized at a much lower iodine content, (*b*) others standardized at 0.3 per cent iodine and (*c*) a variety of tablets which are not of any known or labeled potency, which ought never to be employed. It is highly important that whenever a physician writes his prescriptions for thyroid he should specify the type he prefers to use. There is no such recognized material in American pharmacy as "thyroid extract." Thyroxine is now regarded as a chemical of much interest for research but of no present importance in clinical practice. It is probably of no value to delay the absorption of thyroid or to coat it to avoid action of digestive enzymes, and it is advised that especially coated tablets of thyroid be shunned. He states that it is better clinical practice to give the daily requirement at one regular daily dose and pointed out that maximal benefits (or maximal toxicity) appear only after two months or longer from the initiation of a given dose.

Parathyroid.—This gland substance is not dependably active if given orally. Clinical control of parathyroid tetany can be maintained with ease by use of either vitamin D or a special irradiation product of ergosterol called dihydrotachysterol, and clinicians seldom use the parathyroid extracts.

Pancreas.—Wishful thinking or unwillingness to believe the overwhelming mass of testimony is still responsible for use of pancreatic substance orally.

Adrenal Medulla.—In recent years there has been a series of efforts to make the adrenal hormone have a slow and sustained action. This is being tried by combination of epinephrine with gelatin or by solution of epinephrine base in oil, from which absorption is slower than when the hydrochloride of the hormone is given in aqueous solution.

Adrenal Cortex.—Although there are diverse claims as to the relative effectiveness of various extracts Sevringhaus states that the differences are not great. He suggests employing divided doses two or more times daily. The synthetic steroid desoxycorticosterone is an adequate substitute for some but not all the functions of the adrenals.

Ovaries.—It is Sevringhaus' belief that the older ovarian preparations should have been entirely eliminated since development of newer materials. Because of inactivation after oral administration of the three natural estrogens, relative costs have operated against this use of any except estrone, and even this product has not been prepared in convenient form. Noncrystalline mixtures of the estrogens are not strictly standardized but are active and may be administered by a variety of routes. Comparisons of cost are still difficult. Intramuscular injection of estrogens is often advised because of the slow and prolonged effects, but Sevringhaus points out the following disadvantages: 1. Absorption is not so uniform

as with frequent small doses. 2. The oils too often remain at the site of injection. 3. Some patients have allergic reactions to the oily vehicles.

It seems probable that synthetic estrogens (diethylstilbestrol) will supplant natural ones to a large extent because of their low cost and the high degree of effectiveness on oral administration.

Testis.—Though testosterone is presumably a testicular hormone, testosterone therapy certainly does not provide complete replacement for the activity of the testicles. For oral administration the methyl ester is more satisfactory. The advantages of the inunction route of administration is debatable in the case of either of these materials.

Anterior Pituitary.—Growth-promoting extracts are relatively crude, and it is difficult to estimate the relative potency of various preparations. Neither are the gonadotropic extracts well standardized, but all or most of their activity is also obtained from serum of the pregnant mare. The author favors cyclic administration of the latter product. In contrast, chorionic gonadotropin inhibits the follicular function in women, though it stimulates interstitial cell function in the testicles.

Posterior Pituitary.—The chief uses of these extracts are pharmacodynamic rather than for endocrine substitution (except in diabetes insipidus). Intranasal application of the crude powder is easier, safer and more economical than injection of the aqueous extracts.

Conclusion.—Sevringhaus urges the development of a noncommercial testing laboratory to assure uniform potency, stability and dependability as to type of action of endocrine materials.

LYNCH, St. Paul.

BISMARSEN (BISMUTH ARSPHENAMINE SULFONATE) FOR TREATMENT OF SYPHILIS: A REVIEW OF FOURTEEN YEARS' EXPERIENCE. HERMAN BEERMAN, BERTRAM SHAFFER and CLARENCE S. LIVINGOOD, J. A. M. A. **120**:333 (Oct. 3) 1942.

The authors find that bismarsen is a relatively nontoxic and easily administered drug for the treatment of syphilis. In early syphilis it has a good effect, but it results in slower healing and has a slower spirillicidal action than do other arsenicals. In latent syphilis the reversal of the fixed positive serologic reaction and the prevention of neurosyphilis and other forms of clinical syphilis are effectively accomplished. Bismarsen is a safe and effective drug for the treatment of cardiovascular syphilis. It is not recommended for the treatment of active interstitial keratitis, as its action is too slow. It has a slower healing effect than the other arsenicals in cutaneous and osseous gummatous syphilis. It is not the remedy of choice for neurosyphilis.

THE USE OF BISMUTH COMPOUNDS IN SYPHILOTHERAPY: THE RESULTS OF TREATMENT OF LATENT SYPHILIS BY BISMUTH COMPOUNDS COMBINED IN PART WITH ARSENICALS. DAVID KAHN and S. WILLIAM BECKER, J. A. M. A. **120**:338 (Oct. 3) 1942.

The authors present the results they obtained in the treatment of late latent syphilis by the use of large amounts of bismuth combined with moderate amounts of an arsenical and compare these results with those obtained by the Cooperative Clinical Group. The treatment given by the authors consisted of a minimum of six courses of bismuth subsalicylate in oil (eight to ten weekly intragluteal injections), with rest periods of one month. A course of an arsenical (six to eight intravenous injections at weekly intervals) is given simultaneously with the second, fourth and sixth bismuth courses. Treatment is then continued with courses of bismuth at progressively longer intervals, namely, three months, six months and one year. A yearly course of bismuth is then given as long as the serologic reaction shows any degree of positivity. Kahn and Becker obtained satisfactory

results in 68.5 per cent of their cases. With similar material the Cooperative Clinical Group obtained satisfactory results in but 51.7 per cent of their cases. The patients included by the authors in their investigation of late latent syphilis include those with asymptomatic syphilis who had the disease for three or more years. Kahn and Becker have the impression, on the basis of their results of treatment of 200 patients, that combined bismuth and arsenical therapy is superior to use of the drugs in alternating courses.

BISMUTH HEPATITIS: A SURVEY OF ONE HUNDRED AND TWENTY-ONE CASES. GEORGE V. KULCHAR and WILLIAM J. REYNOLDS, J. A. M. A. **120**:343 (Dec. 3) 1942.

Jaundice, particularly during the bismuth phase of treatment for syphilis, has been a frequent occurrence among the prisoners in the state prison at San Quentin, Calif. Of the 1,032 inmates receiving treatment between July 1, 1936 and Jan. 1, 1942, 144, or 13.9 per cent, became jaundiced one or more times during the course of treatment. In 121, or 10.3 per cent, of these the hepatitis occurred while bismuth was being given, the remainder receiving either an arsphenamine or tryparsamide at the time jaundice was first noted. Neoarsphenamine or mapharsen was given in courses of ten weekly injections in alternation with iodobismitol with saligenin in courses of twenty weekly injections. The patients were all males. The authors believe that the effect of previous arsphenamine therapy as well as the less evident factors of diet, alcoholism and intercurrent infection all predispose the liver to damage from bismuth. While they do not deny the importance of predisposing factors, nevertheless it is their opinion that the primary cause is the bismuth itself.

HENSCHEL, Denver.

PILI TORTI HEREDITARII. B. APPEL and S. J. MESSINA, New England J. Med. **226**:912 (June 4) 1942.

Appel and Messina discuss at length the work of Ronchese on pili torti and point out the error of appending the name of Galewsky to this abnormality. "Pili torti" appeared in print for the first time in July 1932 in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY (Ronchese) and in Jadassohn's textbook (Galewsky). Ronchese's case, however, was presented before the New England Dermatological Society in 1931.

Appel and Messina report the case of a 10 year old girl. The hairs were twisted, thin and brittle. Their tendency to break at a point about 1 cm. from the scalp caused a large area of relative alopecia of the vertex. An older brother, a younger sister, a paternal aunt and a grandmother all had a similar but definitely less noticeable condition. Hence the addition of the term "hereditarii." A moderate degree of keratosis pilaris was noticed on the neck of the girl. The abnormality is considered as an ectodermal dysplasia, and its cause remains unknown.

RATTNER, Chicago.

BACTERIAL FILTRATES IN THE TREATMENT OF CUTANEOUS INFECTIONS. F. C. COMBES, New York State J. Med. **42**:1143 (June 15) 1942.

Combes treated several kinds of cutaneous infections with bacterial filtrates prepared according to the method of Besredka from Staphylococcus albus, Staphylococcus aureus, Staphylococcus citreus, Streptococcus viridans, Streptococcus pyogenes, hemolytic streptococci and Bacillus pyocyaneus. The preparation used was called antipeol. It was applied both in liquid and in ointment form. The treatment was beneficial in cases of carbuncle, furuncle, hydroadenitis axillaris, furuncles of the nostrils and impetigo.

PRURITUS ANI, WITH SPECIAL REFERENCE TO THERAPEUTIC TATTOOING WITH MERCURY SULFIDE. R. TURELL, New York State J. Med. **42**:1335 (July 15) 1942.

Turell discusses extensively the physiology, the causes (systemic diseases, psychic factors, faulty anal hygiene and dermatologic lesions) and the treatment (diet, estrogens, sedatives, psychotherapy, local measures, perianal injections of oil-soluble anesthetics, subcutaneous injections of alcohol and tattooing with mercury sulfide) of pruritus ani.

The technic of the last-mentioned therapeutic procedure was described by the author in a previous paper. He recommends testing the patient first for sensitivity to mercury, an instance encountered only in 1 patient. Gratifying results have been obtained in over 50 patients, followed for more than one year.

IRRADIATION IN INFECTIONS. L. B. GOLDMAN, New York State J. Med. **42**:1341 (July 15) 1942.

Goldman reports the results of roentgen therapy in 640 cases of infections. Of particular interest are the good results obtained in infections of the face, carbuncles and erysipelas.

The dosage used in cellulitis was 100 r (135 kilovolts, 3 mm. aluminum filter and 40 to 50 cm. focal skin distance) repeated in twenty-four hours and again, if necessary, in seventy-two hours. For erysipelas two treatments of 100 r each with a one day interval (100 kilovolts, 40 cm. focal skin distance and 1 mm. aluminum filter). For carbuncles and furuncles he used 100 to 135 r, followed by 100 r in twenty-four hours and 75 r one day later.

EPIDEMIOLOGIC METHODS USED IN THE CONTROL OF VENEREAL DISEASES IN NEW YORK CITY. T. ROSENTHAL and H. GOODMAN, New York State J. Med. **42**:1346 (July 15) 1942.

Rosenthal and Goodman describe the work of the bureau of social hygiene of the city of New York, the filing of the reports, the obtaining of the information, the frequent checking with the physicians to be sure the patients are under treatment, the mailing of the *Quarterly Bulletin* issued by the department of health and the free supply of antisyphilitic drugs. Particular attention is given the premarital and prenatal cases, the children's deaths and the exclusion of children from school. Uncooperative and recalcitrant patients are forcibly hospitalized. Food handlers, barbers, beauticians and masseurs reported as having a communicable form of venereal disease are excluded from work.

SYPHILIS AND CANCER: REPORTED SYPHILIS PREVALENCE AMONG 7,761 CANCER PATIENTS. M. L. LEVIN, L. C. KRESS and H. GOLDSTEIN, New York State J. Med. **42**:1737 (Sept. 15) 1942.

This is the report of a detailed study based on 7,761 cases of cancer reported in upstate New York in 1940-1941.

Of 3,151 white male patients with cancer, 3.2 per cent were found to have syphilis. Of 4,610 white female patients with cancer, 1.7 per cent were found to have syphilis. The highest prevalence of syphilis among males was those with cancer of the tongue, and among females, in those with cancer of the cervix.

In the discussion of the paper Dr. Isadore Rosen agreed that antisyphilis therapy should be given a fair trial in all patients with a positive Wassermann reaction but stated that it should not be extended beyond a few weeks at most, and then not with intensive arsenical medication but with bismuth. He remarked how frequently patients are encountered with extensive syphilitic glossitis, leukoplakia and ulcerations from excessive smoking, jagged teeth and ill fitting dentures, without production of cancer. He expressed the opinion that the use of

intravenous arsenicals is contraindicated in cases of tertiary syphilis with any kind of glossitis or leukoplakia for fear of development of epitheliomatous proliferations.

RONCHESE, Providence, R. I.

THE INCIDENCE OF SYPHILIS IN A MALE GONORRHEAL CLINIC. HERBERT H. COWPER and FREDERICK G. NOVY JR., Urol. & Cutan. Rev. **46**:431 (July) 1942.

The authors noted that 12.8 per cent of patients entering the Oakland Venereal Clinic for gonorrhea also have syphilis and that approximately half of them have early syphilis. It was further shown that repeated blood tests are necessary, for 13.8 per cent of those with syphilis had a negative reaction on entry.

THE PREVENTION OF NITRITOID REACTIONS FOLLOWING TRYPARSAMIDE THERAPY. SAMUEL J. ZAKON and SAMUEL M. BLUEFARB, Urol. & Cutan. Rev. **46**:435 (July) 1942.

Nitritoid reactions from the use of tryparsamide are increasing in frequency. These reactions are preceded by other evidences of hypersensitivity, especially of the gastrointestinal type, and when these symptoms occur it is suggested that administration of the drug be stopped.

HYPERKERATOSIS UNGUALIS UNIVERSALIS. ANDREW G. FRANKS, Urol. & Cutan. Rev. **46**:439 (July) 1942.

A case of hyperkeratosis ungualis universalis is described. Four generations of one family are reviewed, in which the tendency for this condition seemed to be dominant, being transmitted through the maternal grandfather and the mother and later by the father. It was not sex linked.

HOW LONG DOES SYPHILIS REMAIN INFECTIOUS? FELIX PINKUS, Urol. & Cutan. Rev. **46**:442 (July) 1942.

The author analyzes the data on 3,047 prostitutes who were observed for fourteen years or more in answering the following two questions: 1. How long does syphilis remain in the infectious stage? 2. How should one explain the exceptionally late occurrence of infectious lesions?

Of the group studied, 2,856 were syphilitic for more than ten years. Fifty-eight, or 2 per cent of these, presented infectious lesions later than ten years after their first infection; 116, or 4 per cent, later than seven years after their first infection. The author considers that persons with old syphilis but with infectious signs have been reinfected or superinfected and that many old prostitutes are just as capable of transferring syphilis as are young, recently infected ones.

SYPHILIS IN PREGNANCY. CHRIS HALLORAN, Urol. & Cutan. Rev. **46**:454 (July) 1942.

The following data are taken from a recent study of the records of syphilitic pregnant women treated at the Los Angeles Maternity Service over a ten year period. Syphilitic pregnant women tolerate treatment better than do the non-pregnant women. The clinical manifestations of early syphilis in pregnancy may be suppressed. The hope for a satisfactory termination of pregnancy in a syphilitic woman is increased in direct proportion to the amount of treatment given her during pregnancy.

THE CHOICE AND USE OF BISMUTH COMPOUNDS IN THE TREATMENT OF SYPHILIS. NORBERT C. BARWASSER, Urol. & Cutan. Rev. **46**:456 (July) 1942.

The author reviews the general indications and contraindications to the use of bismuth, the absorption and excretion characteristics and the various types of bismuth.

Bismuth in some of its forms is indicated in all phases of syphilis unless there is an idiosyncrasy or allergy to the drug.

Bismuth is contraindicated if there is any indication of allergic reaction at the site of injection, either cutaneous or embolic. The occurrence of a toxic dermatitis or exfoliative dermatitis, if precipitated by bismuth, excludes the further use of that drug.

BISMUTH ERUPTIONS IN ANTI-SYPHILITIC THERAPY. RAY O. NOOJIN and J. LAMAR CALLAWAY, Urol. & Cutan. Rev. **46**:458 (July) 1942.

Cutaneous eruptions due to bismuth are rare, and fatalities due to bismuth therapy other than those caused by faulty injection technic are extremely rare. Bismuth eruptions are divided by the authors into two groups, the acute and the chronic. The acute types are erythematous, erythematous exfoliative, scarlatiniform, urticarial and purpuric and the erythema multiforme and herpes zoster types. The chronic types are the pityriasis rosea, lichen planus and lichen simplex chronicus types, fixed eruptions and generalized chronic eczematoid eruptions.

BISMUTH STOMATITIS. FRANCESCO RONCHESE, Urol. & Cutan. Rev. **46**:462 (July) 1942.

The author reports on the favorable use of sodium hexametaphosphate, 15 parts, and talc, 85 parts, in the form of a tooth powder as a preventive of bismuth stomatitis in 5 patients intolerant to bismuth.

PHYTO-PHOTO-DERMATITIS. ROBERT KLABER, Brit. J. Dermat. **54**:193 (July) 1942.

A number of plants or the extracts appear to excite a contact dermatitis only after subsequent exposure of the skin to sunlight. The author suggests the name phytophotodermatitis to include all those eruptions produced by external contact with plants and their extracts after subsequent exposure to light. The importance of the determination of the wavelength responsible for exciting phytophotodermatitis may be deduced from the Grotthus-Draper Law. This states that only those wavelengths which are absorbed by a system can produce photochemical reactions in that system. Conversely, those wavelengths which excite a photobiologic reaction, such as phytophotodermatitis, must be absorbed before they can do so.

If unfiltered ultraviolet rays are substituted for sunlight, the erythema resulting directly from the shorter wavelengths precludes a sufficient dose of the longer rays to excite the phytogenic reaction. It has been shown by a variety of methods that the effective spectral range lies in the neighborhood of the longer ultraviolet bands. The wavelengths responsible within this range have been more accurately determined in the case of the parsnip and fig.

PRELIMINARY OBSERVATIONS ON A DISORDERED FAT METABOLISM IN SOME SKIN-DISEASES. E. C. DODDS, H. MACCORMAC and J. D. ROBERTSON, Brit. J. Dermat. **54**:212 (July) 1942.

The authors observed that there was no constant improvement in 10 patients with psoriasis on a low fat intake and, conversely, that the eruption was not aggravated by a high fat diet. Biochemically the blood cholesterol of a patient with psoriasis is normal. The response to the ingestion of cholesterol by mouth in the subjects studied was normal. The blood cholesterol was estimated by the method of Myers and Wardell.

BLUEFARB, Chicago.

Society Transactions

CLEVELAND DERMATOLOGICAL SOCIETY

C. G. LaRocco, M.D., *President*

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James R. Driver, M.D., *Reporter*

April 23, 1942

A Case for Diagnosis (Tuberculosis Verrucosa Cutis? Verruca Vulgaris?). Presented by Dr. C. L. Cummer and Dr. C. G. LaRocco.

T. M., a Negro aged 27, presented from the department of dermatology and syphilology of St. Vincent Charity Hospital, has an irregular scar situated in the median line about 2 cm. above the tip of the nose. At the upper pole is a verrucous lesion about 1 cm. in diameter, surrounded by a slightly elevated border.

The patient states that he had had a wart or mole on the tip of the nose for several years. In August 1940 he scraped it, as a result of a fall. This was followed by a scar and the appearance of the growth.

The Wassermann reaction of the blood was negative, but because of a positive Kline reaction of the blood antisyphilitic treatment was administered and resulted in no change in the lesion.

Histologic examination of the verrucous lesion showed the epidermis to be thin and regular. There were several degenerated hair follicles and a large number of underlying normal-appearing sebaceous glands. They were interrupted in the midportion of the section by an irregular hyperplasia of squamous epithelium forming irregular projections into the underlying tissue and showing extensive hyperkeratosis. The underlying stroma showed extensive small round cell infiltration, and there were some collections of phagocytosed blood pigment. There was nothing to suggest tuberculosis, and there was no evidence of malignant epithelial change.

DISCUSSION

Dr. E. W. Netherton: I do not believe that the section shown is compatible with the diagnosis of tuberculosis. There are no tubercles seen. I suggest that a culture be made in order to determine if this patient has blastomycosis or some other fungous infection.

Dr. R. E. Barney: To me the clinical evidence is in favor of tuberculosis verrucosa cutis. I suggest that another biopsy be performed.

Poikiloderma Vasculare Atrophicans. Presented by Dr. E. W. Netherton and Dr. George H. Curtis.

J. S., a married woman aged 49, was in good health until September 1940, when she had eight abscessed teeth extracted. Shortly after this the skin on the face became red, scaly and pruritic. The eruption spread rather rapidly over the trunk and extremities. There has been no edema or vesiculation. Unless olive oil or a bland ointment is applied, the skin becomes dry and slightly scaly. In July 1941 she suffered a severe attack of pharyngitis. In August 1941 her tonsils were removed. There have been stiffness and tenderness of the shoulder joints throughout her illness, and at times she has some tenderness in the muscles of the legs and arms. She has lost 15 pounds (6.8 Kg.) during the past year. Her

family history is irrelevant, and the only serious illness which she had in the past was typhoid fever in 1918.

General physical examination showed nothing of importance except the cutaneous eruption and evidence of chronic arthritis and periarthritis, involving the shoulder joints. There apparently is some atrophy of the muscles of the shoulder girdle; this, however, is not great. The eruption involves almost the whole cutaneous surface with the exception of a few areas on the lower extremities and the palms and soles. It consists of large poorly demarcated areas of atrophy, erythema, hyperpigmentation and telangiectasia. These areas are so closely placed that they have become confluent, giving the general appearance of erythroderma of almost a universal type. There are no areas of sclerosis of the skin or signs of an infiltrative process in the corium. The areas of atrophy and telangiectasia associated with the light erythema are especially evident on the dorsal surfaces of the hands, the extensor surfaces of the arms and the chest. The face is entirely involved by this process. There is no thickening of the skin on the dorsal surfaces of the fingers or on the face. There is a distinct limitation of motion of the shoulder joints due to periarthritis. There is also a mild chronic atrophic arthritis involving other joints.

The hemogram, urine, basal metabolic rate and roentgenogram of the chest were all normal. The cholesterol content of the blood was 120 mg. per hundred cubic centimeters, and the sedimentation rate was 1.8 mm. in one hour.

Specimens for biopsy were taken from three separate lesions, one through the earlier more erythematous area which did not show decided atrophy and telangiectasia and two from areas showing various stages of atrophy. In all of the sections more or less the same pathologic changes were noted. There was atrophy of the epidermis, and the interpapillary pegs were completely obliterated. There were several layers of loosely packed hyperkeratotic cells on the surface of the epidermis. The granular layer was absent in places. There was some edema with a mild degree of sapogiosis of the malpighian layer. The basal layer was intact. There was edema in the papillary layer of the corium, and the capillaries in this region were greatly dilated. The vessels were more numerous just beneath the portions of epidermis which showed the greatest degree of atrophy. Some of them were surrounded by a loose lymphocytic infiltration. There were also a few epithelioid cells, large pigment-containing cells and fibroblasts in the perivascular infiltration. There were fragmentation and some basophilic degeneration of the collagen in the upper part of the corium. The elastic tissue was normal. Sebaceous glands were not observed, and there was definite atrophy of the sweat glands.

DISCUSSION

DR. H. N. COLE: I should like to suggest the diagnosis of persistent dermatomyositis. It is true that the eruption also has some of the characteristics of poikiloderma of Jacoby, but there are the profound changes that would be compatible with dermatomyositis. The patient also gives a history of arthritis or myositis in the shoulder girdles, which would go with that disease.

DR. E. W. NETHERTON: Dr. Cole's point is well taken. I should like to point out that in the opinion of some authors chronic dermatomyositis is probably a form of poikiloderma vasculare atrophicans. The same holds true of scleropoikiloderma. I think they should be classified in the same broad group. Our patient also presents clinical evidence of myositis. We presented her with the feeling that the disease is similar to that in the cases reported by Petges and Cléjat under the title of "Poikilodermatomyositis."

Localized Scleroderma. Presented by DR. C. L. CUMMER.

Miss T. C., aged 25, has several lesions on the thighs and posterior surface of the trunk. They first appeared in September 1940; since then others have appeared, and all have increased slowly in size. The smallest is about 1 inch (2.5 cm.) in diameter, the largest about 2 by 4 inches (5 by 10 cm.). They are

circular to irregularly ovoid, shiny, china like, firm, infiltrated and with dusky violaceous borders.

Thyroid has been administered and acetylbetamethylcholine chloride (mecholyl chloride), 0.25 per cent ointment, employed.

The basal metabolic rate on March 21, 1941 was + 19 per cent and on April 15 was + 3 per cent.

DISCUSSION

DR. C. L. CUMMER: I should like a therapeutic suggestion.

DR. H. J. PARKHURST, Toledo, Ohio: I have recently seen a patient who showed decided improvement following the long term administration of corpus luteum.

DR. GEORGE H. CURTIS: This woman told me that she is getting well. She said that these lesions had been whiter, much larger and more boardlike. I believe the disease may continue to undergo involution.

DR. C. L. CUMMER: During the past year there has been a definite improvement in the lesions.

Tinea Amiantacea. Presented by DR. C. G. LAROCCO.

C. C., a white girl aged 19, complains of sores in her scalp of four to five months' duration. She has had the usual diseases of childhood, and general physical examination shows her to be in excellent health. There are seven members in her family, and none of them has a similar disease.

Scattered through the scalp are several irregular, variously sized scaly patches, measuring from 2 to 4 cm. in diameter. A patch on the vertex was raised and rounded like a cocoon and covered with heaped-up yellowish gray asbestos-like scales. Removal of these scales extracted the hairs, and at the same time the scales would cling to the hairs like pieces of torn plaster. The other patches are plaquelike with piled-up scales, pasting the hairs together and seemingly gluing the whole mass to the scalp. There are no follicular pustules or impetiginous crusts.

Microscopic examination of the scales showed no fungi.

DISCUSSION

DR. C. G. LAROCCO: Inasmuch as this disease has not been proved to be caused by a fungus, it would seem that the term pseudo tinea amiantacea is more appropriate.

Neurotic Excoriations. Presented by DR. C. G. LAROCCO.

A. D. R., a white woman aged 45, complains of scars on her face and body for the past ten to fifteen years. She had measles, varicella and scarlet fever in childhood. She has been married eighteen years and has two children living and healthy. There have been six miscarriages.

She frankly states that at times her skin is devoid of pain and that at other times she has an everlasting urge to "dig something" out of her skin and there is no relief until she does.

Most of the face is terribly disfigured by deep irregular scars, some linear and others circular and triangular. Over the scapular area, the upper portion of the chest and the arms the scars are more superficial. At present there are several crusted papules on the arms.

Clinical evidence of syphilis was not found on physical examination. Serologic reactions for syphilis were negative.

DISCUSSION

DR. C. G. LAROCCO: I presented this patient because of the unusually striking disfigurement. She consulted me because her family have grown up and are ashamed of how she appears.

Multiple Idiopathic Hemorrhagic Sarcoma of Kaposi. Presented by Dr. B. F. Barney, Columbus, Ohio.

P. W., a boy aged 16, states that a dime-sized purplish red spot appeared on the outer aspect of the right ankle in the summer of 1937. The lesion slowly enlarged. He consulted several physicians, but no diagnosis was made and treatment was of no avail. In June 1938 he was referred to the State of Wisconsin General Hospital, Madison, Wis., where a diagnosis of Kaposi's sarcoma was made. During the next two years radium treatments were given approximately every six to eight weeks. After this he received three roentgen ray treatments at six week intervals.

A biopsy was performed in December 1941. The histologic picture was not typical of Kaposi's sarcoma. In December and January solid carbon dioxide was applied with firm pressure. The results were unsatisfactory.

The eruption is confined to the external aspect of the foot and the lower third of the right leg. It consists of plaques varying in size from that of a pea to that of a silver dollar and larger. They are irregular in shape and of a violaceous color, which does not disappear on pressure. The plaques are raised about ⅛ inch (0.32 cm.) above the surrounding normal skin and give a distinct sense of infiltration when palpated. Surrounding some of these plaques are pinhead-sized to pea-sized areas of brownish red pigment. There are no lesions elsewhere on the body.

DISCUSSION

Dr. H. J. Parkhurst, Toledo, Ohio: I observed small papules in these patches which gave me the impression of a hypertrophic lichen planus, and I thought the histologic appearance in the slide submitted was suggestive of this disease.

Dr. E. W. Netherton: I favor the diagnosis as presented of Kaposi's disease. Unfortunately the histologic section was too thick, but I thought I could see small hemorrhages and round cell infiltration resembling the histologic structure of this disease. I suggest that a thinner section be cut.

A Case for Diagnosis. Presented by Dr. C. L. Cummer.

S. S., a white man aged 21, a railway fireman, first noted an eruption six or seven years ago. In the left flank, in the right crural area, on the right shoulder and in the right lumbar area are circular to ovoid areas in which are grouped firm nodules and papules, apparently deeply situated in the corium.

These papules and nodules vary in size from that of a match head to that of a small pea. They are round topped with apparently normal intervening skin. In some areas distinct flat white circular scars are seen, which the patient states have followed similar lesions.

Roentgen therapy had been used by a prior medical attendant wtihout appreciable benefit.

The Kahn reaction of the blood was negative. The hemogram was normal.

Histologic examination showed an intact epidermis with little hyperkeratosis and slight irregular thickening of the rete pegs. In the dermis there was a chronic inflammatory reaction manifested by small and fairly large localized collections of proliferating fixed tissue cells especially around small thin-walled blood vessels. There were few migratory inflammatory cells. There was no evidence of tuberculosis.

The histologic picture was that of focal proliferative reaction of fixed tissues rather than of infiltration of inflammatory cells. The reaction was not specific from a histologic standpoint.

DISCUSSION

Dr. R. E. Barney: I had the impression that some of the lesions are distinctly lichenoid papules. Some of them have a follicular distribution. Some of the areas show a certain amount of scaling. The patient states that the erup-

tion does not itch and that treatment has been of no benefit. I believe he has pityriasis lichennoides chronica.

DR. I. L. SCHONBERG: I, too, believe the eruption resembles parapsoriasis, but in addition I think that the possibility of a lymphoblastoma should be kept in mind.

DR. H. J. PARKHURST, Toledo, Ohio: I agree that a lymphoblastoma should be considered.

DR. C. L. CUMMER: The hemogram showed no abnormalities. I was impressed by the infiltration of fixed tissue cells in the corium rather than inflammatory cells.

Keratosis Follicularis. Presented by DR. H. A. HAYNES JR., Akron, Ohio.

G. H. F., a white man aged 41, first noticed roughness of the skin over the shoulders in January 1942. Shortly thereafter irregular dark brown discoloration of the forehead appeared. He ascribed the eruption to an oral cold vaccine which he had been taking. There is no history of other illnesses or medication, and he states that he has had a normal well balanced diet.

The neck, the upper portion of the trunk and the arms present roughness of the skin with a nutmeg grater feeling. Close inspection reveals horny, protruding pinhead-sized follicular plugs. Some are skin colored, and others are a dirty brown, with the color extending around the follicular orifices. The forehead presents an irregular diffuse dark brown pigmentation with slight follicular dilatation in the pigmented zones.

Histologic examination showed a funnel-shaped dilatation of the follicular orifices which were filled with keratotic material. The epidermis surrounding the follicles showed absence of the stratum granulosum and irregular small cells with poorly staining nuclei, the "grains" of Darier. No large *corps ronds* were seen. There were moderate perifollicular lymphocytic infiltration in the corium and slight degeneration of the upper layers of the corium.

During the past month the patient has taken by mouth 100,000 U. S. P. units daily of vitamin A and has used an ointment containing 1 per cent salicylic acid. Definite improvement has resulted.

DISCUSSION

DR. H. A. HAYNES JR., Akron, Ohio: Reports have appeared in the literature on the value of vitamin A in the treatment of Darier's disease. I therefore employed it in this case and believe there has been a definite improvement.

Neurogenic Arthropathy, Result of Bone Graft. Presented by DR. C. G. LAROCCO and DR. C. L. CUMMER.

D. E. P., a Negro aged 59, presented from the department of dermatology and syphilology and of orthopedics of St. Vincent Charity Hospital, has had an enlarged right ankle joint since 1938. He has been a patient at the City Hospital and the Cleveland Clinic Foundation Hospital, and at both institutions a diagnosis of Charcot's joint was made. He also visited another "clinic," where the joint was opened. Since then it has discharged from a fistulous opening.

Continuous treatment of alternating courses of mapharsen and a bismuth compound had been given at the Cleveland Clinic Foundation Hospital from June 14, 1939 to Dec. 17, 1940, and nineteen injections of a bismuth compound were given at St. Vincent Charity Hospital from April 25 to Sept. 5, 1941.

On Nov. 12, 1941 Dr. C. Glenn Barber performed an operation in which a graft about 1 by 5 inches (2.5 by 13 cm.) obtained from the right ileum was inserted into the outer anterior surface of the right ankle, after exposure of the lower portion of the tibia and fibula, as well as the calcaneum.

The graft resulted in a fairly firm fixation of the ankle, and there has been less drainage from the fistula.

The right ankle joint is enlarged in all directions and immobile. There is a sinus with a serous discharge on the left anterior surface.

Serologic reactions for syphilis of the blood and of the spinal fluid were negative.

A roentgenogram made in December 1940, prior to the operation, showed a rather profound destructive change in the ankle joint itself. In the region of the external malleolus there was a large bony defect with apparently complete loss of the bony substance. In addition, there were osteoarthritic changes extending into the soft tissues.

A roentgenogram made in March 1942 showed fusion of the graft with the tibia and the tarsal bones.

DISCUSSION

DR. E. W. NETHERTON: My associates and I gave this man antisyphilitic treatment in 1939 and 1940 with indefinite results. We questioned the diagnosis of Charcot's joint at that time.

DR. C. L. CUMMER: The operation was performed for the purpose of immobilizing the joint. It is too soon to predict the ultimate outcome, but fusion apparently has taken place.

Adenoma Sebaceum. Presented by DR. C. G. LAROCCO and DR. C. L. CUMMER.

M. J. G., a Negress aged 35, presented from the department of dermatology and syphilology of St. Vincent Charity Hospital, has had an eruption on her face since infancy.

There are buckshot-sized to split pea–sized discrete, firm, rounded, deeply pigmented lesions on the entire face but most numerous in the nasolabial folds and on the upper lip. Minute capillaries are seen on the surfaces of some lesions.

Histologic examination showed downgrowths from the overlying stratified squamous epithelium in the form of finger-like projections of neoplastic cells which were of basal cell character. There was a tendency toward pseudoalveolar formation. The exact extent of the tumor penetration could not be determined, but approximately one sixth of the specimen consisted of tumor.

DISCUSSION

DR. H. J. PARKHURST, Toledo, Ohio: I thought that clinically and histologically the disease was multiple benign cystic epithelioma.

DR. H. N. COLE: I agree with that diagnosis.

DR. G. W. BINKLEY: I agree with that diagnosis but noted some areas in the section resembling cylindroma.

C. G. LAROCCO, M.D., *President*

J. E. RAUSCHKOLB, M.D., *Secretary*

JAMES R. DRIVER, M.D., *Reporter*

May 28, 1942

Leukaemia Cutis. Presented by DR. R. E. BARNEY.

S. Z., a woman aged 49, noticed a purplish discoloration on the right shin eighteen months ago. This gradually enlarged to its present size without symptoms. About a year ago she felt a lump in the middle of the inner surface of the right thigh. She has had pain attributed to neuritis in the right arm continuously

for six months. For the past year her diet has been restricted to reduce her weight. Except for having the pain in the arm she feels well.

The patient is rather obese. Involving the middle of the anterior surface of the right shin is a silver dollar–sized slightly elevated firm purplish plaque. In the middle of the inner aspect of the left thigh is a cherry-sized hard nodule attached to the skin. The remainder of the physical examination gave normal results.

A roentgenogram of the chest showed the heart to be moderately enlarged. The hemogram showed 5,000,000 red blood cells and 8,300 white blood cells per cubic millimeter and 14.9 Gm. of hemoglobin per hundred cubic centimeters. The differential count revealed 45 per cent polymorphonuclear neutrophils, 45 per cent lymphocytes, 6 per cent large mononuclear cells, 3 per cent eosinophils and 1 per cent basophils. The urine was normal.

A biopsy of material taken from the border of the lesion over the right tibia showed a slightly hyperkeratotic epithelium. In the lower part of the corium was a widespread irregular infiltration of round cells which showed only slight variation in size. The nuclei were rounded or irregular and lobulated. The majority of cells stained moderately, but a small number stained deeply. Only a small number of cells were oxidase positive. Some of these showed branching pseudopodia and might represent phagocytes.

DISCUSSION

DR. I. L. SCHONBERG: In regard to the hemogram, I should like to know if vital stains were made. There was a lymphocytosis, with 45 per cent lymphocytes, but there was no description of these cells. It would seem to me that further evidence is necessary in order to make a diagnosis of leukaemia cutis.

DR. H. N. COLE: I agree with the diagnosis as presented. The histologic evidence is conclusive. However, the clinical appearance is not so characteristic of this disease. I thought it resembled somewhat certain examples of myxedema that one sees on the legs.

DR. R. E. BARNEY: In answer to Dr. Schonberg, the patient presents a blood picture compatible with leukemia. The white cells are only slightly increased in number. The differential count shows a relative increase in lymphocytes. The blood has been checked repeatedly in the blood study clinic of St. Luke's Hospital and has always presented essentially the same picture.

Xanthoma Tuberosum Multiplex. Presented by DR. R. E. BARNEY.

H. O., a man aged 29, states that yellowish lesions appeared on the back of the neck eighteen months ago. Since that time similar lesions have appeared on the trunk and extremities. There are no subjective symptoms.

He is well nourished and well developed. Involving the middle of the inner aspect of the right arm is a large pea–sized firm yellow papule. Just below and anterior to this is a similar lesion the size of a glass pinhead. Scattered over the trunk, extremities, face and dorsa of the hands are about eighteen similar lesions varying in size from that of a pinhead to that of a small pea. Most of the lesions are yellow, while some are reddish.

The cholesterol content of the plasma was 199 mg. per hundred cubic centimeters. The Wassermann and Kline reactions of the blood were negative, and the urine was normal.

Histologic examination revealed a flattened epidermis. Immediately below the epidermis was an infiltrate of cells consisting of fibroblasts, xanthoma cells and numerous Touton giant cells. The fibroblastic cells formed short bands and in some instances showed a whorled arrangement. The collagen fibers were present at the border of the infiltrate. There were a small number of round cells seen in the infiltrate. A section stained with sudan III revealed fat in the giant cells and xanthoma cells.

Lupus Vulgaris; Squamous Cell Epithelioma; Latent Syphilis. Presented by Dr. R. E. Barney.

D. L., a white woman aged 45, states that she has had an eruption on the right side of her face as long as she can remember. About eight months ago she struck the middle of her right cheek on the corner of a table. A small ulcer developed at this site and has gradually enlarged. For the past three months she has been receiving antisyphilitic therapy from her family physician, consisting of fifteen intravenous and fourteen intramuscular injections, without benefit.

The patient is well developed and fairly well nourished. She presents an eruption involving the right side of the face, extending from just below the lower eyelid anteriorly over the side of the nose, downward under the ramus of the mandible and posteriorly to within 1½ inches (4 cm.) anterior to the ear. The border shows large pea-sized apple jelly nodules which are firm to palpation. The skin in this area shows some atrophy. In the center of the eruption is a silver dollar–sized infiltrated plaque. The border is rolled, everted and pearly, while the center shows several areas of ulceration. On the right side of the neck is a plum-sized group of pea-sized apple jelly nodules. There is a lymph node the size of an olive at the right angle of the mandible.

Histologic examination of a section from one of the nodules on the right side of the neck showed an ulceration of the epidermis. The corium revealed typical tubercles made up of epithelioid cells, lymphocytes and Langhans giant cells. Most of these tubercles were proliferative, while some showed central caseation necrosis.

Biopsy of a specimen taken from the infiltrated plaque in the center of the lupus vulgaris showed a well differentiated, ulcerated, squamous cell epithelioma of the skin.

The Wassermann and Kline reactions of the blood were positive. The hemogram was normal. A roentgenogram of the lungs was normal. A patch test with tuberculin elicited a positive reaction.

DISCUSSION

Dr. J. E. Fisher: The patient presents serologic evidence of syphilis and has apparently had considerable arsenical therapy. I should like to ask the presenter if he believes this treatment responsible for the epithelioma.

Dr. J. R. Driver: Lupus vulgaris is usually classified as a precancerous lesion, and this case illustrates it. However, in many instances previous irradiation has been given for the lupus, and the subsequent malignant change is often attributed to this treatment. In this case no irradiation had been given, and therefore the patient presents an excellent example of the precancerous nature of lupus vulgaris. Trauma, a factor that probably plays a part in such cases, is also present.

Dr. R. E. Barney: I do not think the treatment that the patient had received, which apparently was with one of the arsenicals and a bismuth compound, has anything to do with the development of the epithelioma. It is a recognized fact that when there is a break in the continuity of the skin or mucous membrane it is a likely site for the development of a malignant lesion. I think that is the case here. There was lupus vulgaris lasting a long time, and there was a break in the continuity of the skin and in that area a squamous cell epithelioma developed.

A Case for Diagnosis (Erythema Multiforme?). Presented by Dr. R. E. Barney.

G. S., a white woman aged 40, complains of a sore throat which began Dec. 19, 1941. In February 1942 a diagnosis of Vincent's angina was made and all the teeth were removed. The gingivitis subsided, but the mouth and tongue remained sore. There is occasional improvement, but the condition never entirely disappears. At times the eyelids share in the eruption. There is pain on swallowing, and

there have been occasional periods of hoarseness. Her diet has been varied and liberal. She has no gastrointestinal complaints. From time to time small "pimples" appear on the face, arms and trunk. She has lost 22 pounds (10 Kg.) in six months. Her hair has been falling for the past two months.

The patient is fairly well developed and well nourished. There is a generalized thinning of the hair on the scalp. The face shows a few small pea-sized subacutely inflammatory crusted papules. On the trunk is a subacutely inflammatory papular dermatitis of pinhead-sized lesions. The mouth shows pinhead-sized to large pea-sized erosions on the buccal mucosae, especially just anterior to the anterior tonsillar pillars. The dorsal and ventral surfaces of the tongue, the anterior and posterior tonsillar pillars, the soft palate and the pharynx show a similar process. In these areas, as well as the mucosa of the lower lip, an occasional small pea-sized acutely inflammatory vesicle is seen. The patient has been taking vitamins, sodium salicylate and sulfathiazole. Intramuscular injections of thiamine chloride, thio-bismol and a foreign protein have also been administered.

The Wassermann reaction of the blood was negative. The urine was normal.

Scrapings from the right buccal mucosa showed staphylococci and streptococci.

The hemogram showed 4,320,000 red blood cells and 9,000 white blood cells per cubic millimeter. The hemoglobin amounted to 11.2 Gm. per hundred cubic centimeters. The differential blood count showed 54 per cent polymorphonuclear leukocytes, 31 per cent lymphocytes, 7 per cent mononuclear leukocytes, 6 per cent eosinophils and 2 per cent basophils. The sugar content of the blood was 91 mg. and the urea nitrogen content 9.4 mg. per hundred cubic centimeters.

DISCUSSION

DR. H. J. PARKHURST, Toledo, Ohio: It struck me that in a case of this sort with recurrent lesions in the mucosa and conjunctiva the possibility of pemphigus should be kept in mind.

DR. H. N. COLE: I thought there was one lesion on the lip that was annular and rather suggestive of an annular type of erythema multiforme. I favor a diagnosis of erythema multiforme. The patient is apparently perfectly well otherwise.

DR. J. R. DRIVER: The condition in this case resembles somewhat a form of toxic erythema described by Klauder and others under the name of ectodermosis erosiva pluriorificialis (ARCH. DERMAT. & SYPH. **16**:1067-1097 [Nov.] 1937). The involvement of the eyes and the extensive eruption in the mouth are suggestive of this.

DR. R. E. BARNEY: At present this patient has lesions on the vocal cords. She has presented that picture before. The lesions extend and involve the entire oral cavity. I thought of the possibility of pemphigus, but in the cases of pemphigus that I have encountered the course of the disease has been rapidly downhill, and usually the lesions are blood crusted at some time. And, as Dr. Cole pointed out, the nutrition is usually poorer than that of this patient.

NOTE.—The following report on this patient was made by Dr. R. E. Barney on Oct. 22, 1942:

I presented this case as one of erythema multiforme, and most of the members agreed with the diagnosis as presented. I treated the patient with all the common things used for that condition, but she became progressively worse and lesions developed on the body. She was admitted to the hospital. The eruption changed from the picture of erythema multiforme of the bullous type to what apparently, clinically, was dermatitis herpetiformis. During the last two weeks of her life the picture of typical pemphigus developed, and she died on October 16.

Circumscribed Myxedema (Localized Solid Edema of the Extremities in Association with Exophthalmic Goiter [O'Leary]). Presented by DR. R. E. BARNEY.

A. K., a Negro aged 53, was referred to the department of dermatology and syphilology of St. Luke's Hospital on Nov. 28, 1941 for examination of an erup-

tion on the legs. In February 1940 symptoms of a toxic goiter had developed, but it was not until April 1941 that a partial thyroidectomy was performed. At this time the basal metabolic rate was + 66 per cent. A second operation was performed on June 9, 1941, and since that time he has been feeling well. In August 1940 the right leg, from the foot to the inguinal region, became swollen to twice its normal size and was hot and painful. The swelling subsided in four days. In July 1941 the legs began to swell during the day but returned to their normal size during the night. After a month the swelling became permanent, although even now it decreases somewhat at night. There is an occasional slight shooting pain in the legs associated with a feeling of heaviness and stiffness.

The patient is well nourished, well developed and apparently in good health. Both legs are swollen, the right more than the left. The skin of the legs from just below the knees to the ankles reveals a boardlike induration with some increase in temperature. The skin in the involved areas resembles a pig's skin, and over the tibias there is a papillomatous hypertrophy. There is a firm cherry-sized nodule over the right internal malleolus. The ankle, feet and toes share in the swelling. The skin over the dorsa of the feet is indurated and shiny. There is a bilateral, shotty, painless, pea-sized to almond-sized inguinal adenopathy. There is a keloid at the site of the thyroidectomy.

A roentgenogram of the chest on March 30, 1942 showed healed primary calcified tuberculous complex, occupational fibrosis and chronic pulmonary emphysema.

The Wassermann reaction of the blood was negative. The urine was normal. The basal metabolic rate on May 5, 1942 was + 17 per cent.

A biopsy was performed on a specimen from the outer aspect of the right leg at the junction of the lower and middle thirds. The skin was lined by a hyperkeratotic, acanthotic epithelium containing abundant pigment. In the upper part of the corium there was a zone in which there was fragmentation of the collagen presenting a myxomatous appearance. There was a focal infiltration of round cells.

Best's carmine method of staining showed a fine pink-staining fibrillar material in the myxomatous zone already described.

DISCUSSION

DR. E. W. NETHERTON: This man presented several features that are not characteristic of localized myxedema. There was a verrucous or papillomatous surface that is seen in elephantiasis. I had the impression that there was a definite lymph stasis. The small nodules and papules on the toes and scattered over the surface of the legs are unlike those seen in localized myxedema. In myxedema there are light brown or pinkish plaques with orange-peel-like or pigskin-like dimpling around the follicles. It is usually softer and not as firm as this. There is difficulty in suturing the wound made for obtaining a specimen for biopsy because the skin tears so readily. Histologically, the myxomatous change under the epithelium is more evident than in this case. In this case another histologic change which is not seen in cases of localized myxedema is the hypertrophy of the skin. It is thick and dense, such as would be seen in elephantiasis. I believe this man has elephantiasis with some myxedematous degeneration in the skin.

DR. H. N. COLE: On being questioned carefully this man gives a clearcut history of having had a swelling in his right groin, after which his leg swelled to about twice the normal size and he had fever and was very ill. I think that the elephantiasis present can be explained on the basis of lymph stasis and venous obstruction. This same condition may be seen in connection with certain other diseases. I have seen it in 3 patients with old tertiary syphilodermas. It has also been seen in connection with lupus vulgaris. There is no question about this clearcut history of a toxic goiter, but I am inclined to agree with Dr. Netherton that the patient does not have myxedema.

DR. R. E. BARNEY: The swelling of the leg from the ankle to the thigh subsided entirely, and after this he complained of the leg's swelling during the day and subsiding at night until finally it reached the stage where it remained swollen. At the time the specimen was taken for biopsy the myxomatous material welled up in the incision and one could string it out. I feel that the history and picture now present could fit in with the diagnosis as given.

Malignant Melanoma. Presented by DR. R. E. BARNEY.

E. D., a white woman aged 44, states that she had had a brown dime-sized "mole" in the right groin as long as she can remember. About the middle of March 1941 the "mole" began to increase in size and turn pink. It was removed on March 29, 1941. Two months later she noticed two lumps in the right groin. These were removed on June 19, 1941. After this tumors gradually developed in the right groin, right breast and left axilla and under the clavicles. There is a moderate amount of pain in the right shoulder. She has lost 12 pounds (5.4 Kg.) in the past year. A panhysterectomy was performed in December 1940.

There are three plum-sized to orange-sized tumors in the right inguinal region. The largest tumor shows an ulcerated vegetative surface with an associated foul-smelling discharge. The other two tumors are purplish and show softening. Over the right anterior iliac portion of the spine are a lemon-sized similar tumor and a small cherry-sized nodule. The subcutaneous tissue underlying these tumors is diffusely infiltrated. The skin over the lower portion of the abdomen shows scarring, hyperpigmentation and atrophy. There is a half-palm-sized infiltrated plaque over Scarpa's triangle on the right side. Involving the lower outer quadrant of the right breast is a firm plum-sized subcutaneous tumor. Just under the inner end of each clavicle is a cherry-sized firm nodule. There is a plum-sized shiny purplish tumor with central softening in the left axilla.

Examination of the urine showed no melanin. A roentgenogram of the chest on Jan. 14, 1942 showed no evidence of metastasis. The Wassermann reaction of the blood was negative.

The nevus was removed on March 29, 1941. Histologic examination showed hyperkeratosis and an extensive papillary infolding of the epidermis. In addition, the epidermis showed large masses of pigment. The corium revealed clusters of nevus cells which showed a moderate degree of pigmentation. Adjacent to this area was a moderately well defined tumor. This was roughly spherical and made up of polygonal cells having abundant cytoplasm and chromatic nuclei. These nuclei showed slight variation in size, shape and staining quality, with an occasional mitotic figure. The arrangement of cells was trabecular. In some of these cells occasional masses of pigment were seen. The cells were supported on a moderately well vascularized, rather scanty connective tissue stroma. There was an epithelial pearl just under the epidermis. The tumor was not encapsulated, and, while there was no evidence of invasion of the underlying corium, there was a moderate degree of round cell infiltration at the periphery of the tumor.

Histologic examination of a lymph node in the right inguinal region on June 18, 1941 revealed a metastatic malignant melanoma.

DISCUSSION

DR. B. F. BARNEY, Columbus, Ohio: This patient presents an excellent example, which is too often seen, of inadequately treated primary melanotic lesions. Wide surgical excision of melanotic moles from such areas before malignancy develops is necessary if one is to prevent such a hopeless situation as this patient presents.

DR. J. R. DRIVER: This woman gives an interesting history and not an uncommon one in cases of melanoma. She had a brown mole in the right groin present since birth, and several days before its removal she noted some elevation of the lesion. There was no ulceration or bleeding before its removal for histologic examination. Had the pigmented mole been removed before growth had

started it is likely that no further trouble would have resulted. However, since growth in the lesion had begun, there was definite evidence of a melanoma. Therefore, removal of the lesion merely for histologic purpose was contraindicated. The procedure indicated was wide, deep excision of the primary lesion and block dissection of the regional lymph nodes. The surgical removal of flat black or brown pigmented moles from areas that may be subjected to trauma is the best type of surgical prophylaxis against cancer.

A Case for Diagnosis. Presented by DR. G. M. STROUD.

M. G., a 44 year old housewife, presented from the department of dermatology and syphilology of the University Hospitals, complains of a red swelling of the center of the face for six months. She began to gain weight at about the age of 23 and reached over 200 pounds (90 Kg.) when she was 35. In recent months she has lost 40 pounds (18 Kg.). There were no menses between the ages of 25 and 35. Normal rhythm then returned, but during the past year the menses have been very irregular. She has never been pregnant. Fairly generalized hirsutism has been present since the age of 16. Her appetite has usually been excessive. Polydipsia and polyuria have existed for many years. Since an automobile accident five years ago, in which she sustained a head injury followed by coma for about twelve hours, she has been nervous.

About six months ago a pustular eruption began on the center of the face. Two months ago swelling of this region, particularly of the lower lip, began. The skin became purplish red and telangiectatic in places. There has not been much attendant discomfort.

The hair on the scalp is slightly scanty, particularly over the frontal regions and occiput. There is moderate hirsutism, which is noticeable on the face. There is a fairly well defined, edematous, slightly indurated, relatively nontender purplish red telangiectatic eruption of the center of the face, extending from the upper lip, which is maximally swollen, to the lower eyelids. The area blanches moderately on pressure and is scaly and crusted in places. There are no oral lesions. The tonsils are moderately enlarged. Several firm, discrete, nontender, submandibular and anterior cervical lymph nodes are present.

The urine and hemogram were normal. The Kline reaction of the blood was negative. The fasting blood sugar was 254 mg., the plasma cholesterol 157 mg., the serum calcium 11 mg. and the phosphorus 3.8 mg., per hundred cubic centimeters of blood. The blood phosphatase was 6.1 units. Scrapings from the cutaneous lesion revealed no fungi in a fresh preparation. Culture for pyogens revealed beta hemolytic Staphylococcus aureus. The basal metabolic rate was + 13 per cent. The tuberculin test, with 0.1 cc. of 1:1,000 old tuberculin intracutaneously, resulted in a 1.5 by 1.5 cm. area of erythema and edema after twenty-four hours.

Roentgenograms of the skull showed questionable areas of destruction in the right parietal bone and definite destruction, or osteoporosis, of the anterolateral portion of the wall of the left maxillary sinus. A roentgenogram of the chest was normal, while one of the abdomen showed bilateral renal calculi and a possible left ureteral calculus.

Histologic examination of the cutaneous lesion showed large fairly well circumscribed nests of epithelial cells with necrotic centers in some of them. In some of these nests there were degenerated polymorphonuclear cells and lymphocytes were scattered about. This granulomatous infiltrate, which was chiefly in the corium, had invaded the fat. The epithelium was not contained in the histologic section. No tubercle bacilli were revealed by acid-fast stains.

During the patient's stay in the hospital she had a mild degree of fever.

DISCUSSION

DR. B. F. BARNEY, Columbus, Ohio. The patient's condition clinically resembles rhinoscleroma. The histologic picture is definitely that of a granuloma.

DR. E. W. NETHERTON: I believe this patient's condition belongs in the sarcoid group. The induration is not as great as one sees in rhinoscleroma.

DR. I. L. SCHONBERG: The eruption is inflammatory and developed in a comparatively short time. Also, roentgenograms showed some questionable osseous changes. I should consider the diagnosis of chronic inflammatory edema of the face.

DR. J. A. GAMMEL: Have any of the sulfonamide drugs been administered? The inflammatory reaction in the lymph nodes makes me favor a diagnosis of a low grade streptococcic infection.

DR. H. N. COLE: I favor a diagnosis of sarcoidosis, as suggested by Dr. Netherton. Some features of the eruption resemble lupus vulgaris. Further study of the case is indicated.

DR. R. E. BARNEY: I, too, favor a diagnosis of sarcoid and thought the histologic evidence compatible with this diagnosis.

DR. G. M. STROUD: I favored the diagnosis of a pyogenic inflammatory disease and have planned to administer sulfathiazole. Roentgenograms of the small bones of the extremities have been made, but the report has not been received.

Hairy Tongue. Presented by DR. R. E. BARNEY.

A. F., a white man aged 26, noticed hairlike projections on the tongue one year ago. There are no associated subjective symptoms. In the beginning this eruption would come and go, but for the past few months it has been present constantly. The projections can be scraped off but tend to recur.

There is a dark brown hairlike eruption on the posterior third of the center of the dorsum of the tongue. The color is most pronounced in the center of the patch, fading toward its borders.

Histologic examination revealed moderate parakeratosis and acanthosis of the epidermis with numerous papillary projections. Clusters of bacteria were seen. The papillary layer of the corium revealed a slight round cell infiltration.

PHILADELPHIA DERMATOLOGICAL SOCIETY

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April 17, 1942

Atrophy of the Optic Nerve: Rapid Progress. Presented by DR. J. V. KLAUDER.

C. S., a white man aged 28, stated that he has never had syphilis and has had no antisyphilitic treatment. His wife is 21 and has never been pregnant. Prior to his marriage, four years ago, the Wassermann reaction of his blood was negative. He came to the hospital first in March 1942, because of failing vision, which was first noticed in October 1941. At this time he went to an optician for glasses, which did not improve his vision. He was able to work as a waiter until the time of his first visit to the hospital. His visual acuity was: right eye, perception of hand movements; left eye, 6/60, with considerable contraction in the field for form. The optic nerves are now white; the pupils are irregular and react sluggishly to light. The patellar reflexes are decreased and unequal. The ankle reflexes are active and unequal. The Wassermann reaction of the blood was 4 plus, and the spinal fluid was syphilitic in all phases (cell count, 2 lymphocytes per cubic millimeter; globulin [moderate]; Wassermann reaction, 4 plus, and colloidal gold curve, 1112231000).

Juvenile Tabes with Atrophy of the Optic Nerve. Presented by DR. MARJORY K. HARDY.

J. D., a white boy aged 10 years, presents large, irregular pupils which do not react to light. The patellar and ankle reflexes are absent; the gait is normal. Ophthalmoscopic examination showed the media to be clear. The fundi showed bilateral primary atrophy of the optic nerve with diminution in the caliber of the vessels. Slit lamp examination revealed no evidence of interstitial keratitis. The child was admitted to a general hospital in September 1940 for treatment of "acute cystitis." A routine Wassermann test was found to elicit a strongly positive reaction. Treatment was started in October 1940. In May 1941 poor vision was noted in school. At that time the vision was: right eye, 6/15; left eye, 6/30. The fields for form were contracted. The child is below the normal weight and height for his age. The facies is suggestive of congenital syphilis; the bones, joints and teeth are normal. The patient's father is living and well and has a negative Wassermann reaction of the blood. His mother is living and well but has a positive Wassermann reaction of the blood. She is receiving antisyphilitic treatment. Three brothers, all older than the patient, are living and well and have negative serologic reactions for syphilis. The patient's Wassermann reaction has remained strongly positive. Examination of the spinal fluid in March 1941 and again in December showed: globulin, none; Wassermann reaction, negative, and colloidal gold curve, 0000000000. To date the patient has received thirty injections of mapharsen, each 0.02 Gm., and thirty-two injections of 1.5 cc. each of bismuth subsalicylate in oil (57 mg. of elemental bismuth per cubic centimeter).

Atrophy of the Optic Nerve; Congenital Syphilis. Presented by DR. J. V. KLAUDER.

R. D., a white man aged 26, the oldest of two brothers and one sister, first complained of impaired vision two years prior to his admission to the hospital in March 1942. He went to an optician, who prescribed glasses which seemed to help him for one year. He then consulted his physician, who gave injections in the arm for about one year before referring him to an ophthalmic hospital. On admission his visual acuity with correction was: right eye, 3/60; left eye, 6/60. The nerve heads are pale. The pupils are dilated and fixed to light. The patellar and ankle reflexes are exaggerated and unequal. He has the facies of congenital syphilis and Hutchinson teeth. The Wassermann reaction of the blood was 4 plus, and the spinal fluid was syphilitic in all phases (cell count, 2; reaction for globulin, weakly positive; Wassermann reaction, 3 plus, and colloidal gold curve, 1111000000). The diagnosis is congenital syphilis with cerebrospinal involvement and atrophy of the optic nerve.

DISCUSSION OF THREE CASES OF ATROPHY OF THE OPTIC NERVE

DR. J. V. KLAUDER: These cases are a remarkable example of the age range of atrophy of the optic nerve in congenital syphilis. One point worthy of emphasis is the delay in early diagnosis of atrophy of the optic nerve because of patients' consulting opticians. Again, there is often delay in a patient's being referred to the proper place to receive modern treatment, after he realizes that the optician cannot help him. Unfortunately, a certain percentage of the patients on their first visit to Wills Hospital are already eligible for pensions for the blind. This is important in the attack on blindness caused by syphilis. The man of 26 is one of the oldest patients I have ever seen with atrophy of the optic nerve caused by congenital syphilis. It is interesting to note that he does not have tabes. He was inoculated with malaria, but unfortunately it did not "take." In the case of the man with acquired syphilis and atrophy of the optic nerve it is a question whether fever therapy will be of any help, since the atrophy is too far advanced. The little boy with congenital syphilis has typical tabes as regards objective neurologic signs, but it is not typical inasmuch as he has a normal spinal fluid.

DR. JOHN H. STOKES: I do not believe I could add anything to what Dr. Klauder has said. What puzzles me about cases like these sometimes is: Has any one seen progression of the contraction of the field and increase in the atrophy after the reaction of the fluid has become negative and remained so for some time? I have just encountered a case in which this took place.

DR. J. V. KLAUDER: I am under the impression that there are such occurrences. Normal spinal fluids are seen, which do not correlate with the optical findings.

DR. JOHN H. STOKES: What will be the ultimate fate of the older patient?

DR. J. V. KLAUDER: Ordinarily such a patient becomes blind and just disappears from observation. It is planned to give the little boy malaria therapy, and I think it will offer him more chance of keeping the disease nonprogressive.

DR. SIGMUND S. GREENBAUM: Since you cannot tell whether the disease is going to progress or not, I think that is the only thing left to do.

DR. MARJORY K. HARDY: I think that the lesson to be learned from the case of the little boy is the importance of making an ophthalmoscopic examination. When this child was first seen in a general hospital, it was noted in his physical examination that he had irregular pupils, nonreactive to light. In spite of that, a normal spinal fluid, to the hospital attendants, ruled out any complications, and therefore nothing else was done until the child actually had failing vision. Another interesting point in his history is that from the time he was 2½ years old until he was 5 he smoked a cigar a day. When he came to the ophthalmic clinic, nicotine was considered to be the cause of the atrophy of the optic nerve.

DR. SIGMUND S. GREENBAUM: Schamberg and I in one of the first articles published in America on malarial therapy of neurosyphilis (*Atlantic M. J.* **30**:554 [June] 1927), mentioned the case of a child with tabes who could not walk into the hospital but who walked out of the hospital a few weeks after the malarial therapy was terminated. In selected cases such therapy may be of great value.

DR. CARROLL S. WRIGHT: A child with dementia paralytica whom my associates and I treated was normal for several years and even went to school after malarial treatment. How far she went in school I do not know.

DR. DONALD M. PILLSBURY: This is certainly not the usual experience with children with neurosyphilis.

Herpes Zoster (of Traumatic Origin). Presented by DR. J. V. KLAUDER.

M. L., a white man aged 65, while engaged in his work as a bricklayer, on April 8 felt a piece of hard mortar blow into the left eye. There was an immediate stinging sensation and thereafter a sensation of a foreign body in the eye. After the accident he was examined by a physician, who could not find a foreign body but made a diagnosis of laceration of the upper left lid under the cilia. On the morning of April 10 an eruption appeared on the forehead. It was not preceded or accompanied by pain; the only sensation was that of itching. I first saw the patient on April 16. There was a typical eruption of herpes zoster with subsiding vesicles on the forehead in the midline running from the base of the nose to about 1 inch (2.5 cm.) past the hair line. There is evidence of a healing laceration on the upper lid of the left eye, just below the cilia.

DISCUSSION

DR. J. V. KLAUDER: Is there a relation between the herpes zoster and the trauma from the standpoint of workmen's compensation laws? The herpes zoster as a possible sequela of trauma is not important in this case, since it does not involve the eye and no loss of vision will result. Otherwise, it is relatively unimportant. I am convinced that there is a relationship of trauma and herpes zoster. I was amazed at the number of cases reported in the foreign literature, many of the authors subscribing to a relationship. Curiously, no case has been

reported in the English literature. Many writers think that the occurrence of herpes zoster after trauma is evidence of an ascending infection of the nerve by the virus introduced at the site of trauma. Considering the many curious things that viruses produce and the relationships of virus diseases to other diseases, I feel that the development of herpes zoster after trauma is more than coincidence (Amman, E.: Herpes zoster ophthalmicus traumaticus, *Klin. Monatsbl. f. Augenh.* **95**:793, 1935).

Lupus Erythematosus (Combined with Lupus Vulgaris?). Presented by Dr. A. Strauss and Dr. Isadore Zugerman.

J. C. B., a white man aged 63, was treated twenty-three years ago for lupus erythematosus. At that time he was to have received gold sodium thiosulfate but did not return to the clinic. On Jan. 27, 1942 the patient had a prostatectomy. During hospitalization his skin improved so much that all the erythema disappeared. When he was discharged all the symptoms and signs returned. Clinical examination reveals a large atrophic area on both cheeks and forehead. Covering almost the entire atrophic area is an infiltrated erythematous eruption. The blood counts and the results of chemical examination of the blood and urinalysis were normal. The Wassermann reaction of the blood was negative.

Lupus Erythematosus. Presented by Dr. J. P. Guequierre.

L. S., a Negress aged 28, has had lupus erythematosus of the scalp for several years. Administration of ascorbic acid produced decided reduction of telangiectasis and tenderness in one week.

DISCUSSION OF CASES OF LUPUS ERYTHEMATOSUS

Dr. John H. Stokes: I should be inclined to say that the diagnosis of lupus erythematosus is inclusive enough to take in the whole picture, especially in the light of previous irradiation. My observation of the effect of irradiation on erythematous lupus has been so unfavorable that I am prepared to find pagetoid changes in the atrophic residue of lupus erythematosus and epitheliomatous changes, chronic eczematoid premalignant processes, and so on, without feeling that I have to bring lupus vulgaris into the diagnosis. That elevated edge which sometimes makes one think one is dealing with epithelioma is a "trick" manifestation of this process, and only biopsy can determine whether one is dealing with a superficial, self-healing epithelioma or an actively indurative type of erythematous lupus.

Dr. A. Strauss: As far as I am aware, our patient never had any roentgen ray therapy.

Dr. John H. Stokes: I should like to emphasize that in all types of erythematous lupus the response to rest is something one ought to avail oneself of more, therapeutically. Over and over again I have seen this disease improve and almost clear under a rest regimen; and that applies to discoid eruptions quite as much as to disseminate. In Dr. Guequierre's case I was not wholly convinced of the diagnosis of lupus erythematosus. I thought the condition might be pseudopelade in a Negress, extraordinary as that may seem.

Dr. J. P. Guequierre: She has had the eruption for seven years.

Dr. John H. Stokes: A patient can have pseudopelade for seven years.

Dr. J. P. Guequierre: When I first saw the patient she had ulceration and extreme tenderness. I did not think the diagnosis was lupus erythematosus at that time, but later I came to that conclusion.

A Case for Diagnosis (Tuberculosis Cutis? Chronic Pyogenic Dermatitis?). Presented by Dr. Herman Beerman and Dr. Louise E. Tavs (by invitation).

E. R., a Negress aged 40, well developed and fairly well nourished, presents elephantiasis vulvae, a granulomatous perianal eruption and multiple draining sinuses. Twelve years ago the perianal eruption began, associated with draining

sinuses. Five years ago the patient had an operation for removal of "piles," with recurrence of the lesions. One year ago the patient noted temporary recurrent vulvar swelling. Six months ago the vulva remained enlarged. In the past five years the patient has had aching pain in the right lower quadrant of the abdomen, more severe since September 1941. She has had diarrhea and tenesmus in the past five years, associated with mucus and blood in the stools. In the past year she has lost 20 pounds (9.1 Kg.). Medical examination revealed "diminished vesicular breath sounds." Proctoscopic examination showed numerous discharging sinuses about the anal orifice. Digital examination revealed a rather thickened and hard anal sphincter. Sigmoidoscopic examination showed no abnormalities for 20 cm. The patient's brother died of tuberculosis one month ago. The serologic reactions of the blood were negative. The reactions to intracutaneous Frei tests with chick embryo antigen (lygranum) were negative. A Frei test with human antigen gave a negative reaction. Complement fixation tests with the chick embryo antigen gave negative reactions. Reports on guinea pig inoculations and cultures for tubercle bacilli are not yet available. Bacteriologic examination revealed a large number of hemolytic staphylococci (Staphylococcus aureus), a moderate number of colon bacilli, a small number of nonhemolytic streptococci, Streptococcus viridans and an occasional hemolytic streptococcus. There was 80 per cent hemoglobin in the blood. A blood count showed 3,970,000 erythrocytes and 8,350 leukocytes, with 78 per cent polymorphonuclear leukocytes, 21 per cent lymphocytes and 1 per cent eosinophils. Donovan bodies were not found. A roentgenogram of the chest revealed a possible apical lesion. The patient has been given sulfathiazole ointment, sitz baths in saline solution and sulfonamide compounds by mouth.

DISCUSSION

DR. HERMAN BEERMAN: We made the provisional diagnosis of tuberculosis histologically, and Dr. Weidman concurred with that diagnosis today.

DR. SIGMUND S. GREENBAUM: There is a good deal of pruritus in the area, according to the patient's own story, and I am inclined to think that much of the process is the result of friction, rubbing and scratching. She may have a tuberculous infection, but certainly I think a good deal of the condition now present is analogous to hypertrophic lichen simplex of Vidal.

DR. JOHN H. STOKES: I was inclined to feel that this whole process could be explained by the secondary pyogenic infection that occurs in hypersusceptible persons at almost any site of previous trauma or infection, particularly, of course, a fungous infection. It is possible, as Dr. Greenbaum suggests, that the tuberculosis is secondary. At the time I saw the patient she had not been adequately investigated for the locus of the tuberculous infection.

Hemangioma. Presented by DR. DONALD M. PILLSBURY.

S. K., a white boy aged 1 year, was first seen by me at the age of 4 weeks. There was a large, firm hemangioma involving the lower lip and the adjacent portion of the chin, with two linear extensions downward from lateral angles of the mouth and scattered, slightly raised hemangiomatous lesions of varying sizes on the anterior surface of the neck. Spontaneous ulceration of the vermilion border of the lower lip had occurred, and this healed without treatment other than use of a mild ointment. Since superficial roentgen therapy (Chaoul contact technic) has been given the erythematous angiomatous element of the nevus has become less evident. There remains a decided increase in size of the lower lip and adjacent part of the chin.

DISCUSSION

DR. G. E. PFAHLER: The treatment was given with the Chaoul tube. I think the child had 900 r in a period of about nine months, which is not heavy treatment. Apparently, however, there has been some improvement. There has been a great deal of pigmentation—more than I have ever seen—but the child is dark skinned and that is probably the explanation. I have had my best results in using filtered radium, employing 1 mm. of platinum. I do not know that that

is necessary, because good results have been obtained with various types of filter. I suspect that one could continue to get improvement in the lesion along the neck with the Chaoul technic, but it would seem to me that one is not likely to get sufficient penetration in the thick part of the lip. I should insert radium needles for about two hours, putting them in carefully and parallel. This would shrink up the vessels on the inside with relatively little effect on the skin. In a child one may have some trouble in putting the needles in, but they will stay there, once they are in.

One can also get a shrinkage of tissue by surface application of radium. A general rule is to use approximately the same distance that is indicated by the estimated thickness of the tissue involved. I should estimate that the thickness of the tissue in this case is about 2 mm., excepting the lip, so that if a distance of about 2 mm. were used for the application—or 3 mm., so as to get better distribution—shrinkage of the area down along the neck would occur; and insertion of radium needles into the lip would shrink that down. One should then wait two or three months before doing anything more. The first effect I should look for is increased pallor, with decreased color of the area involved.

DR. DONALD M. PILLSBURY: I should say that there has been a definite increase in the pigmentation since Chaoul therapy was given. There has been a definite improvement as far as the superficial angiomatous element goes, particularly on the neck. There has been little decrease in the thickness of the lip, and it seems to have become somewhat more fleshy. One gets the feeling that possibly there are other than angiomatous elements in the lesion of the lip—possibly a good deal of connective tissue.

DR. R. P. BARDEN (by invitation): I think Dr. Pfahler's suggestion about the interstitial use of radium is good. It seems to me that radium seeds might be a little easier to insert and keep in place in a child of this age. I think it may be necessary eventually to consider plastic surgery, but I think irradiation should be given a full chance first.

DR. DONALD M. PILLSBURY: Irradiation and time.

DR. G. E. PFAHLER: I should not attempt any plastic operation inside of two years. I believe that a pretty strong effect would be obtained from inserting radium seeds. I have inserted needles in children of this age. One must bind their hands, but the needles can easily be kept in place for two hours. An hour and a half might be enough.

DR. CARROLL S. WRIGHT: I have nothing further to offer. I recently reviewed this subject in the literature and agree with Dr. Pfahler that if one is to use roentgen radiation it must be of a type which will give deep penetration. The general opinion is that one must produce what amounts to deep endarteritis in order to obtain any effect. From what I know about Chaoul therapy, I understand that the effects are relatively superficial.

DR. G. E. PFAHLER: The first patient I treated was a patient of Dr. Hartzell's, in 1908, and the lesion disappeared, so that now there is no sign left. The site of the lesion looks like perfectly normal skin. I have at present a patient under observation who had an angioma involving the right ear and the entire right side of the head, extending down the right side of the neck. It was associated with a tumor-like infiltration in the neck sufficient to compress the trachea so that it could be shown roentgenographically and so that Dr. Clerf performed a bronchoscopy to see whether he could find any obstruction. The pressure, however, was all from the outside. The child had an associated ulceration of the external auditory canal. It was a hideous thing. Today practically all of that has disappeared, so that a few small blood vessels, looking like telangiectases, are all that is left of that mass. I saw the child first in January and started treatment in February. I did not want to start, because I did not see any hope, but the parents insisted. This case now illustrates how sensitive such lesions are and how they do respond. I made local applications of radium over the surface lesions and then tried to control the tumor mass in the neck by high voltage rays filtered through copper.

DR. DONALD M. PILLSBURY: Every one emphasizes the importance of getting irradiation started early in the treatment of hemangiomas. Can you assign any age after which irradiation will not have a satisfactory effect on the hemangioma?

DR. G. E. PFAHLER: I do not believe there is any such age, but, according to the literature the age of 5 or 6 months is considered the most suitable for treatment. The child I refer to was 4 months old when I saw her. The younger children respond more quickly. The tissues are more sensitive in children, so that they respond to one half or one third of the dose required for an adult.

Congenital Ectodermal Dysplasia; Pachyonychia Congenita? Presented by DR. CARROLL S. WRIGHT.

I. L., a white boy aged 12 years, at birth showed roughening of the entire cutaneous surface and "infection" of the thumb nails. When he was 2 weeks old blisters formed on the soles, knees and elbows. These ruptured and crusts formed. The nails of both hands and feet became infected. The patient was treated for years by various practitioners and at several hospitals in Philadelphia. On May 17, 1937 the patient was admitted to the surgical service of the Johns Hopkins Hospital with the diagnosis of "chronic eczema secondarily infected, producing an impetiginous picture." This was treated with azochloramid compresses and with potassium permanganate and gentian violet; the ulcerated lesions were cleared of infection and remained improved for six months following discharge. They have since progressively become worse, especially during the four months prior to his admission, on April 28, 1940. The only observations of significance related to the skin and mucous membranes. The picture was one of chronic illness and apathy. There was a bronze tint to the skin with exaggeration of the papillae. There were small roughened, keratotic tags projecting from the cutaneous surface. On the trunk and extremities there were a number of large infected areas. These were covered by large, scaly crusts. The feet and perioral region were most severely affected. The tongue, gingiva and buccal mucosa revealed a diffuse superficial leukoplakic involvement. The tip of the tongue was shiny and atrophic.

In 1940 the blood contained 100 per cent hemoglobin (14.5 Gm.) and there were 10,000 leukocytes, with a normal differential count. The urine was normal. The serum protein content was 5.9 Gm. per hundred cubic centimeters. The albumin-globulin ratio was 1.3. The serum cholesterol content was 161 mg. The basal metabolic rate on one occasion, when conditions were not completely satisfactory, was + 40 per cent. Roentgenographic examination of the gastrointestinal tract after the ingestion of barium sulfate was normal. A scraping from the skin was negative for fungi. The Wassermann reaction of the blood was negative. The reaction to a tuberculin test was negative to 0.1 Gm. The patient was treated at Johns Hopkins Hospital with the application of saline compresses. Crusts were removed and denuded infected areas healed with the application of gentian violet or 5 per cent ammoniated mercury. This therapy satisfactorily cleared old lesions of infections. An attempt was made to pare down the nails with a scalpel after soaking them in acetone.

Pachyonychia Congenita. Presented by DR. CARROLL S. WRIGHT and DR. E. R. GROSS.

T. N., a white infant girl aged 6 months, presents heavy thickening of all the nails, the thickening increasing toward the free borders. The nail plates are hard and brittle. There is also a leukokeratosis of the tongue. There is a strawberry nevus on the right buttock. The changes of the nails and tongue have been present since birth.

DISCUSSION OF TWO CASES OF PACHYONYCHIA CONGENITA

DR. CARROLL S. WRIGHT: I made a tentative diagnosis of pachyonychia congenita in the first case. The picture includes the changes of the mucous membranes, the nails and the skin, all of which are typical. The patient also shows a cutaneous picture which suggests Darier's disease somewhat. For the cutaneous lesions I think one might use the method described by Dr. L. C. Goldberg (ARCH.

DERMAT. & SYPH. **36**:331 [Aug.] 1937) with a cysteine preparation, and the other treatment might be administration of massive doses of vitamin A. I had never seen an example of this disease until I saw the infant.

DR. JOHN H. STOKES: I have been perplexed a good deal by the alleged avitaminoses. The 12 year old boy is an instance of avitaminosis, although there is not much evidence for it in the history. The first thing that directed my attention to the absorption question was the work of Scott on senile vaginitis and the effect of achlorhydria on the absorption of vitamin A. I think there is a field of investigation well worth while in a case of this sort in the direction of absorption possibilities. Nobody seemed to think that the boy had any great difficulty in getting about in the dark. There is such a thing as congenital achlorhydria. There are also persons with congenital defects in metabolism which might interfere with the utilization of vitamin A; so I should think it would be well worth while to see what can be done with a child of this sort by giving vitamin A by mouth, in conjunction with hydrochloric acid, and giving it in conjunction with other vitamin therapy. I do not know whether there is a satisfactory parenteral way of giving it. An oil-carried vitamin is not a good preparation for parenteral use, but perhaps there is some way to get around the difficulty presented by the intestinal route.

DR. THOMAS BUTTERWORTH, Reading, Pa.: The baby—the second patient—was born with greatly thickened nails. Sometimes patients are born without nails at all. Apparently, finger nails never develop. The baby showed the only typical feature not presented by the boy; that is, it had thin hair on its scalp; the boy had a good growth of hair.

DR. SIGMUND S. GREENBAUM: I showed this patient at a meeting about seven or eight years ago in Harrisburg. It is curious that the baby has merely the pachyonychia, while the older boy had at that time this white, spongy nevus described some years ago by Cannon, who at that time did not connect it with the Jadassohn nail dystrophy (ARCH. DERMAT. & SYPH. **31**:365 [March] 1935). If this baby had a vitamin A deficiency, one would expect to see other changes. Originally that was a miliaria impetigo, in my opinion. On the back there are a number of pustules, and on the buttocks the lesions had developed still further in that there was a distinct bullous streptococcic impetigo. The parents told me that the cutaneous lesions would come and go, and I think it was because the part had been heavily wrapped up that the impetigo has developed on the miliaria.

DR. CARROLL S. WRIGHT: The baby was treated by the family physician from birth for a supposed thrush of the mucous membranes. The child had no lesions on the skin when I saw her about a month ago. I agree that the rash is probably a miliaria, but the lesion on the lower part of the back could conceivably be of the same type, but to a lesser degree, that the boy shows on his feet.

DR. JOHN H. STOKES: One is accustomed to think of one of the clinical features of avitaminosis A as a pyogenic susceptibility on the skin in that crops of pustules and impetiginous processes develop, which are a reflection of avitaminosis in the exaggerated susceptibility of these plugged hair follicles to pyogenic infection. I think Frazier was the man responsible for the original suggestion and based his impression on his observation of the Chinese.

DR. DOUGLASS A. DECKER, Allentown, Pa.: Part of the original description by Jadassohn is the presence of bullae on the skin.

Pemphigus Foliaceus. Presented by DR. JOHN H. STOKES and DR. JOHN W. LENTZ.

G. B., a white woman aged 42, presents a generalized eruption which in its typical phase is of a bullous and exfoliative type. In addition, on April 17, 1942 she had a vegetative, pedunculated, lemon-sized lesion removed, which previously had been diagnosed by biopsy as a basal cell epithelioma. The eruption had its onset following the extraction of an infected tooth. It has persisted for twenty-three years. The present eruption has never completely disappeared. The symp-

toms are a recurrent severe burning sensation and occasional pruritus. The eruption is characterized by unexplained, nonseasonal, recurrent acute exacerbations during which there appear oozing bullae, vesicles, pustules and finally heaped-up crusts and scales. The patient has a chronic infection of the tonsils and a chronic hyperplastic ethmoiditis. The teeth are normal. There is diabetes on the maternal side of the family. There are asthma and urticaria on both maternal and paternal sides. A brother and a sister have goiter. Routine fungous cultures and other studies gave negative results. Blood counts and the urine were normal. No iodides or bromides were found in the urine. Blood sugar and blood urea nitrogen were normal. The most interesting finding was pure cultures of long chain hemolytic streptococci from the skin. The Wassermann reaction of the blood was negative. Previous treatment has consisted of local compresses, baths, olive oil soaks, ultraviolet irradiation, an unknown amount of roentgen irradiation and arsenic by mouth, all given previous to her coming under our observation. In view of finding hemolytic streptococci in culture of the skin, a trial of sulfanilamide in full therapeutic doses was carried out. Clearcut improvement followed. The gastrointestinal reactions, however, necessitated discontinuance of this treatment.

DISCUSSION

DR. JOHN H. STOKES: The patient has had this eruption a long time for pemphigus foliaceus. She illustrates that even in cases of the more hopeless pemphigoid dermatoses something can be done now with sulfonamide compounds in increasing the comfort and prolonging the lives of the patients by cleaning up the hemolytic pyogenic infections from which they suffer. We have had the experience that, while not striking at the cause, we have made several patients with various types of chronic pemphigus more comfortable. This patient could not take sulfanilamide for long periods, but she improved decidedly from it. To me the most interesting thing about her was the epithelioma that developed. The onset in this woman's case is one that I dare say you have observed a number of times—it came on after surgical trauma. It commonly starts around appendectomy wounds, after dental extractions, and so on, and that, to my mind, points to its being a septicemic type of infective process. That was the thing that led me to try sulfonamide compounds as soon as they became available.

DR. A. STRAUSS: How do you account for the seasonal variation?

DR. JOHN H. STOKES: It is difficult to account for it. The perspiration, which is more profuse in summer, gets more alkaline; secondary infections of various kinds do better in summer time than in winter. She might be allergic; and also the tendency to go on an alkaline ash diet in summer makes some patients with this condition definitely worse. They eat an overabundance of fruit and stop eating meat; their skins are hydrated; their carbohydrate intake is increased, because they never think of fruit as sugar, and pyogens flourish in such a background. In the fruit-restricted diet of the winter months they get better. I might mention the curious and inexplicable good effect that the intravenous use of thiamine chloride has on pemphigoid processes, particularly dermatitis herpetiformis. If one wants an alternate for arsenical medication in case of severe dermatitis herpetiformis, 50 to 100 mg. of thiamine hydrochloride may be given intravenously every day or every other day. Of 3 or 4 patients for whom I have tried that, 2 have been strikingly benefited, and the necessity for the use of arsenic was eliminated. The others had severe headache, and the therapy had to be given up. One patient has been under treatment for a year and a half with three injections a week for practically that entire time. He was on the edge of suicide before, his physician said. When he stops taking the drug more lesions appear; there is no cure, but it seems to do something that keeps him comfortable. The physician made one attempt to substitute large doses by mouth, but it was not effectual.

DR. DONALD M. PILLSBURY: Do you plan on using any other sulfonamide compound in treating this woman? It might be worth while to try sulfadiazine (2-[paraaminobenzenesulfonamido]-pyrimidine). I have had the experience in cases like this, in which hemolytic streptococci are not causative but are an important secondary factor, that it has not been necessary to administer large doses.

It is surprising how comfortable some of these patients are when taking small doses of such drugs over a long period of time, doses of 0.5 to 1 Gm. daily.

DR. J. M. SCHILDKRAUT, Trenton, N. J.: I have observed 2 patients with pemphigus who have been cured with sulfadiazine. In 1 the disease was of the vegetating type. To the latter patient I gave roentgen ray therapy to some extent. The dosage of sulfadiazine was not high, 2 Gm. daily. In both of these cases the disease was of long duration, one about two years and the other fourteen months. Arsenic, the Davis treatment and vitamins had no effect. There has been no recurrence in either case, and it is over four years since recovery. Neither patient, however, was a person of Eastern Europe. One woman was born in England, and the other was of English descent.

DR. SIGMUND S. GREENBAUM: I remarked several months ago that vegetative lesions in pemphigus can be cleared up with the oral administration of sulfathiazole. I believe the vegetating lesions in pemphigus are secondary infections and not primarily related to the pemphigus itself.

A Case for Diagnosis (Photosensitization Pigmentation? Melanosis of Riehl?). Presented by DR. CARMEN C. THOMAS and DR. MARJORY K. HARDY.

E. R., a white woman aged 45, presents symmetrically distributed retiform brown-red pigmentation of the sides of the neck, the lower sides of the cheeks, the back of the neck and the "V" of the chest. The upper region of the front of the neck, just under the chin, is uninvolved. The eruption began on the right side of the neck in 1939 and has spread slowly but continuously since. On questioning, the patient admits the local application of toilet water to the involved sites for a period of years, but also to parts of the face which are not involved. She had a "nervous breakdown" four or five years ago but otherwise has been well. The tongue is smooth and the papillae generally atrophic. She has been taking vitamin B complex for some time.

DISCUSSION

DR. A. STRAUSS: Is this condition perhaps a perfume dermatitis with some pigmentation following it?

DR. SIGMUND S. GREENBAUM: I do not think that this condition is entirely pigmentary. Much of what one sees disappears under pressure, indicating the congestive nature of the lesion. If it were the result of photosensitization, pigmentation of varying duration would be apt to be the only result. However, telangiectases like these are fairly common in blonds. One sees them in varying degree all along the neck in the region below the ears, particularly in women. I should classify this patient's condition as poikiloderma of Civatte.

DR. DONALD M. PILLSBURY: I agree with Dr. Greenbaum.

A. STRAUSS, M.D., *Chairman*

DONALD M. PILLSBURY, M.D., *Secretary*

May 15, 1942

Squamous Cell Epithelioma Arising in Old Tuberculous (?) Ulcer. Squamous Cell Epithelioma Arising in Old Radiodermatitis. Presented by DR. C. C. THOMAS.

Z. R., a white man aged 71, presents a palm-sized ulcer in the right axilla. The base shows granulation tissue; the border is sharply defined and slightly rolled. The underlying axillary structures are apparently not involved, and free

motion of the arm is possible. The patient has had pulmonary tuberculosis since 1926 and has had care in a sanatorium for a number of years. The sputum occasionally contains tubercle bacilli, and there is possibly tuberculous laryngeal involvement. The patient has had diabetes since 1938. The lesion in the right axilla began as a pinhead-sized nodule in 1934, while the patient was in a sanatorium. It was cauterized and improved temporarily, but one year later an ulcer developed. The patient was then treated at another hospital with roentgen rays and other (ultraviolet?) radiation weekly for eighteen months, but with constant increase in the size of the ulcer. He was then treated at another hospital, where two biopsies were performed, the second four weeks ago. The histologic report was prickle cell epithelioma. He has been given local applications of a cod liver oil type of ointment, with moderate regrowth of epithelium near the lower border.

DISCUSSION

DR. DOUGLASS A. DECKER, Allentown, Pa.: I saw this patient once, about a year ago. At that time there was no clinical suggestion of prickle cell epithelioma; it was thought that the ulcer was a microaerophilic streptococcic ulcer of the type described by Meleny. I am amazed to see that the lesion has not changed appreciably in the year since I have seen it and also that it is a prickle cell epithelioma. The cancer may have developed in the chronic ulcer recently.

DR. G. E. PFAHLER: Seeing the patient now, I should not hesitate to make a clinical diagnosis of epithelioma. The treatments carried out over a period of eighteen months probably consisted of small doses of roentgen rays on the basis of the lesion's being an inflammatory (tuberculous?) process. Even though the patient was treated for eighteen months, he was possibly given 10 or 15 per cent of an erythema dose once a week—not many doses or many roentgens. The patient practically recovered from any effect between one week and the next, and the lesion therefore kept on growing. Of course, I do not know what the lesion was in the beginning, but I think it could easily have been an epithelioma, and electrocoagulation would be unsuccessful if one did not destroy the entire lesion, as it would simply spread underneath. At present there is a histologic diagnosis. I did not palpate the lesion, and I do not know that any one can decide positively whether the glands underneath are involved or not. With a squamous cell epithelioma one certainly would have to suspect that the deeper glands were involved. If the problem were up to me, I would destroy the lesion thoroughly with electrocoagulation. Working in the neighborhood of axillary vessels, one would have to proceed carefully, but it could be done. I should then treat the area thoroughly with irradiation, with 3,000 or 4,000 r, and should administer this within three or four weeks. I would not give even that much irradiation if I could be reasonably certain that all the lesion had been destroyed by electrocoagulation.

DR. FRED D. WEIDMAN: I am responsible for stirring up all this discussion, in having the courage, I suppose, to say that this lesion is a prickle cell epithelioma instead of pseudoepitheliomatous hyperplasia. I still find it difficult to differentiate between those two conditions, but in this case I feel sure that the lesion is cancerous. When I saw the patient this evening I was uncertain for a moment about my histologic diagnosis, until I saw a certain portion of the uppermost part of the lesion, where pearly epitheliomatous tissue was visible. I think the condition is like that which one sees in old scars and burns in which ulcers develop. That does not necessarily mean that cancer will be present in every part of the margin of the lesion.

DR. THOMAS BUTTERWORTH, Reading, Pa.: How much is the chance of cure increased by electrocoagulation? What is the chance of cure with roentgen rays alone, and what with the combination therapy? Is the difference worth while?

DR. G. E. PFAHLER: In the first place, there is a history in this case of an indefinite amount of irradiation that has been given. I did not see any effects to indicate that roentgen rays had been given. It is known that when a patient

has received small, ineffective doses of radiation over a long period the cancer cells develop resistance to roentgen rays; there is usually associated considerable fibrous tissue and one would have to administer a destructive dose if cure were to be obtained with irradiation alone. If I were treating with irradiation alone, I should use radium, enough to destroy the tissue with a cauterizing effect. I should say that the chance of cure would be doubled with electrocoagulation followed by irradiation.

Cutaneous Syphilis Associated with Lymphoblastoma. Presented by Dr. Sigmund S. Greenbaum and Dr. Bertram Shaffer.

S. L., a white man aged 65, of healthy appearance, presents numerous infiltrated papular and arciform, slightly scaling lesions on the trunk and upper extremities. A few atrophic patches are present on the left side of the face. The right side of the face is slightly swollen. A large node is palpable at the angle of the jaw on the right side. Swelling of the right side of the face began about four months ago. The eruption began twenty-five years ago. The patient had a penile lesion in his youth. Blood counts, the urine, the blood urea nitrogen, the blood sugar and a roentgenogram of the chest were normal. A roentgenogram of the sinuses showed numerous small areas of erosion in the frontal bone, suggesting carcinoma. The reactions to serologic tests of the blood for syphilis were positive on two occasions. A report on a biopsy of the lesion on the cheek was either Hodgkin's disease or reticulum cell sarcoma. The administration of 2,000 r of roentgen rays over a period of three weeks produced 90 per cent involution of the lesion on the cheek.

DISCUSSION

Dr. Herman Beerman: How did the presenters make the diagnosis of cutaneous syphilis?

Dr. Bertram Shaffer: Clinically I made a diagnosis of cutaneous syphilis. The Wassermann reaction was subsequently found to be strongly positive on two occasions. Previous to my diagnosis a diagnosis of Hodgkin's disease or reticulum cell sarcoma was made, which was followed by treatment with roentgen rays. After irradiation the lesion on the cheek underwent almost complete involution. Does this man really have Hodgkin's disease, or is this eruption a manifestation of syphilis, or does he have latent syphilis and Hodgkin's disease of the skin?

Dr. Fred D. Weidman: It seemed to me that these lesions were not particularly dusky; they were pale. They have been present for twenty-five years. I know they are arciform, but, after all, generally in late syphilis are not the arcs larger than these? In syphilis, with such large numbers of lesions, one would expect more ulceration. There is an adenopathy such as would not be present in late syphilis. With all this, I thought there was a good deal in the clinical findings that argued against syphilis.

Dr. Bertram Shaffer: If the disease in this case is not syphilis, I should like to have an opinion as to what it might be.

Dr. Herman Beerman: I should like to know what it is, too. Clinically I was not impressed with a diagnosis of syphilis, because none of the characteristics of late syphilis are present except arciform configuration.

Dr. Fred D. Weidman: Perhaps the patient has Schaumann's disease, in which, as you all know, there is sometimes a parotitis with generalized lymphadenopathy. I think that the amount of change shown in the sections is not commensurate with the degree of infiltration shown in the lesions clinically. Perhaps when sections are cut deeper in the block, more information will be gained. I must say that the changes in the cheek look like sarcoma, but conditions are not suitable tonight for the study required in this case. Pro tem, I should say that the possibility of sarcoidosis should be investigated. This patient has

clusters of nodules at the inner canthus of the eye, such as have been seen in a number of cases of sarcoidosis.

DR. HERMAN BEERMAN: I think there were some tuberculoid structures in the lower portion of the section.

Disseminated Pseudoxanthoma Elasticum. Presented by DR. GEORGE C. GRIFFITH (by invitation) and DR. JOSEPH V. KLAUDER.

W. A., a white man aged 55, was admitted to the hospital because of nervousness, insomnia, anorexia, loss of weight and diverticulitis. The patient is unable to state when the cutaneous disease first appeared; he says that it began "years ago" and that it has become worse during the past ten years. A photograph taken when he was aged 31 shows lesions of the disease on his neck. A photograph of his father taken at the age of 59 shows the disease on the neck. The patient has no knowledge of his grandfather. The patient's son and two daughters do not have the disease. It is distributed over the entire neck, the abdomen, the lower part of the sides of the chest, the lower part of the back over the sacrum, both cubital spaces and the lower anterior surfaces of the thighs. The skin of the neck, the lower part of the abdomen and the sides of the chest is yellowish. It is thin, loose and soft and can be stretched for about 1 inch (2.5 cm.). On the sides of the chest the skin lies in folds, comparable to that of pups of large hounds. On the upper portion of the neck there are a number of irregularly shaped papules that are characteristic of pseudoxanthoma elasticum. On the thighs and in the cubital spaces the process is less pronounced. In these areas the skin is yellowish and is not loose or folded, and there are prominent follicles, presenting the appearance of swine skin. Both fundi exhibited angioid streaks of the retina. An ophthalmologist who examined the patient in 1935 observed such lesions at that time.

DISCUSSION

DR. JOSEPH V. KLAUDER: The disease in this patient is unusually disseminated, almost generalized. I have never seen such widespread involvement of the skin.

DR. FRED D. WEIDMAN: The case is extraordinary in that almost rhinoceros-like folds of skin have developed. I think that the folds have come about as a result of the extensiveness with which the elastic tissue has been deposited in the skin. Some of it has resulted in the formation of striae—I saw some on the neck, after a searching examination—but the proliferation is so massive that for the most part the skin is involved diffusely. The spaces between the ordinary striae have been filled in, and the skin has had to buckle up, so to speak, in order to accommodate this great mass of elastic tissue. The conspicuousness of the depressed follicles is probably due to the pushing up of this elastic tissue between their tissues.

Ichthyosis with Secondary Pyoderma. Presented by DR. DOUGLASS A. DECKER, Allentown, Pa.

S. R., a white man aged 34, shows typical ichthyosis on both legs from the hips to the ankles. Scattered over these areas there are superficial bullae and heaped-up yellow crusts. The ichthyosis has been present since birth; infection developed two years ago. One aunt and two nephews of the patient have ichthyosis. Culture of material from a bulla showed Staphylococcus albus. Mild local therapy produced no change. On Oct. 8, 1941 the patient was given 0.5 Gm. of sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) four times a day, with rapid healing of the infection. This was continued until April 24, 1942. In two days infection recurred.

DISCUSSION

DR. THOMAS BUTTERWORTH, Reading Pa.: This patient is a member of an eastern Berks County (Pennsylvania) family that has overflowed into Lehigh

County and which I have been investigating. About a year ago I presented a pair of twins from this family. Apparently in cases of this disease there are two elements. One is a peculiar form of ichthyosis which seems to affect the extremities almost exclusively, sparing the palms. I do not believe it is a congenital ichthyosiform erythroderma. Accompanying that is what may be classified as epidermolysis bullosa of the simplex type, because bullae arise on hyperkeratotic areas and become secondarily infected and crusted. Dr. Decker's experience with sulfathiazole internally has been repeated by me with local application of the drug. It alleviates the symptoms but has no effect on the prevention of subsequent bullae. In the cases I have encountered the bullae have continued to occur about the knees, ankles and wrists, points of possible increased trauma. It is an interesting family, and time will be needed to gather all the necessary information on it.

DR. DOUGLASS A. DECKER, Allentown, Pa.: I have seen a nephew and a niece of this patient in my office with the same kind of cutaneous lesions. The boy's mother has ichthyosis but does not get secondary infections.

DR. THOMAS BUTTERWORTH, Reading, Pa.: An interesting feature of the eruption in this particular family is that often the bullae cease to develop but the ichthyotic process continues. Some of the patients have shown definite improvement in the bullae during pregnancy. I have an idea that the longer they live, the less likely they are to have bullae develop. One branch of the family has 17 children, 8 or 9 of whom are affected. Everything points to this condition's being a dominant characteristic.

Interstitial Keratitis of the Right Eye Developing After a Full Quota of Treatment and Four Years After Involvement of the Left Eye. Presented by DR. MARJORY K. HARDY.

R. M., a white girl aged 15, had interstitial keratitis of the left eye, which developed in April 1938. Shortly after, antisyphilitic treatment was started. From then until June 1940 the patient received thirty-nine injections of neoarsphenamine and sixty injections of a bismuth compound. Three weeks ago the right eye became injected. There are no stigmas of congenital syphilis except an unusually high palate. The left eye is now clear. The right eye shows pericorneal congestion. The cornea is hazy. The iris is swollen and muddy looking. Slit lamp examination showed: right eye, active interstitial keratitis; left eye, old interstitial keratitis. The Wassermann reaction of the blood has remained positive. The patient is now being treated with pyrifer (a mixture of nonpathogenic fever-producing bacteria).

DISCUSSION

DR. J. V. KLAUDER: One usually thinks of involvement of the second eye in interstitial keratitis as the result of lack of treatment or of insufficient treatment. I do not believe treatment has much to do with it. One sees involvement of the second eye usually within the first few weeks, in a certain per cent of cases within the first few months and in some instances after as long as many years. I had a patient in whom the second eye became involved eight years after the first eye. It appears that treatment is not the deciding factor. I think that inevitably the second eye becomes involved. I do not think interstitial keratitis is ever a unilateral disease, regardless of treatment (Klauder, J. V., and Vandovere, E.: Analysis of 532 Cases of Interstitial Keratitis with Particular Reference to Standardization of Treatment, *Ven. Dis. Inform.* **22**:307, 1941).

Generalized Late Syphilid. Presented by DR. JOSEPH V. KLAUDER.

M. H., a Negress aged 54, was first seen in February 1942. She presented an eruption on the trunk and extremities which first appeared in September 1941. The eruption consisted of discoid plaques, circinate and kidney-shaped lesions, nodules and excoriated eczematous lesions. The edges of some lesions were raised

and infiltrated. Their sizes varied from that of a split pea to that of a palm. The itching disturbed the patient's sleep. She had an attack of hemiplegia in May 1941 but has since recovered to a considerable degree. She attended the neurologic clinic. Tablets of triple bromides were prescribed, which she took for seven months, a daily dose of 60 grains (4 Gm.). About twenty years ago she received a series of injections. The reason for this treatment was not known to the patient. The Wassermann reaction of the blood was negative; the reaction to a Kline test was doubtful at one time and 2 plus at another. Examination of the blood for bromides was reported to give negative results. Bismuth subsalicylate in oil, 2.5 cc. (each cubic centimeter contained approximately 57 mg. of elemental bismuth), was injected weekly, and potassium iodide was given orally. After the second injection there was an appreciable improvement, and there was complete retrogression of all lesions after the seventh injection. The results of histologic examination were reported as follows: "There is a diffuse, infiltrative, hematogenous dermatitis of the utmost severity. The walls of larger blood vessels exhibit evidence of toxic changes amounting almost to necrosis; there are an extreme hyperplasia of the blood capillaries and a high grade of perivascular edema. Around the blood vessels the picture is that of a high grade inflammatory reticulosis. The changes are regarded as toxic rather than bacterial, in view of the absence of leukocytic reaction. Mycosis fungoides may be excluded, in view of the absence of the infiltrate in the papillae, the nonparticipation of the epidermis and the absence of polymorphism in the infiltration. Spiegler-Fendt sarcoid can be eliminated because the lymphocytes are distributed so systematically on the reticulum and around the blood vessels. Syphilis can be excluded."

DISCUSSION

DR. JOSEPH V. KLAUDER: This case is interesting from the standpoint of the conflict between the clinical evidence and the histologic picture. It seems to me that one must remember that just one section was made, at one place. Clinically one gets the entire view of the disease; histologically one looks at one section from one place. May that not possibly explain the conflict?

DR. FRED D. WEIDMAN: I saw this patient previously at a presentation before a group of graduate students. As I recall it, for a long time there was a question whether she had syphilis or not, even in the mind of Dr. Klauder. Now, for some reason or other, Dr. Klauder concludes that she has syphilis. However, it may also be some disease such as rheumatic dermatosis, erythema elevatum diutinum or granuloma annulare, in association with which the patient may have syphilis and a positive Kline or Kahn reaction or other evidence of the disease. I want to submit this: When in and around the blood vessels of the skin there appears a severely inflammatory, toxic reaction, it is not the kind of reaction that is consistent with syphilis. I should like to ask Dr. Klauder whether there is anything else, apart from a 1 plus reaction to a precipitation test and the response to bismuth therapy, to support the diagnosis of syphilis in this case. If not, I would submit that if there is a feeling that the sample of skin selected for biopsy was not representative, why, in the meantime, were some additional biopsies not performed?

DR. JOSEPH V. KLAUDER: The lesions cleared up so promptly that there was no time to perform more biopsies. Retrospectively, my diagnosis of syphilis is based mainly on the fact that the eruption so promptly disappeared after bismuth therapy. What made it unusual was that it was a generalized teritary lesion. One could visualize it as a late syphilid. She certainly had lesions clinically suggestive of syphilis, and they disappeared promptly after bismuth therapy, so I think the diagnosis is reasonable.

DR. DOUGLASS A. DECKER, Allentown, Pa.: At the time I studied this patient, there was a question of bromoderma. When I saw her tonight I went into her history again previous to her attendance at a neurologic clinic for paraplegia, and she stated that she got the same medicine from her previous physician that

she received from the neurologic clinic. I think, therefore, that when Dr. Klauder stopped giving the bromides she got better.

DR. J. V. KLAUDER: The laboratory reported absence of bromides in the blood.

Sarcoidosis. Presented by DR. MARJORY K. HARDY.

E. W., a Negress aged 38, thin, appearing younger than her given age, presents numerous small and moderate-sized soft papules around both eyes. There are a few lesions on the lobes of the ears and similar larger lesions on the lips. There is a large nonpainful swelling involving the lower portion of the nasal septum. This started three months ago following a cold in the head. There are two small papular lesions on the back of the neck. The patient's skin was clear until two years ago, when lesions first appeared on the eyelids. The papules became more numerous and increased in size. Lesions on the lips appeared six months ago. Repeated Kline reactions were doubtful. The reaction to cholesterol antigen was negative. The reaction to a tuberculin test with purified protein derivative, first strength, was 3 plus. A roentgenogram of the chest showed many enlarged mediastinal and hilar glands, particularly on the right side. The lungs were clear, and the heart was not enlarged. The diagnosis was hilar mediastinal tuberculosis, probably sarcoid.

DISCUSSION

DR. FRED D. WEIDMAN: I think the patient has sarcoidosis. I should not say that this particular lesion shows the classic histologic picture of sarcoid, but it is compatible with the diagnosis. I suppose I have been influenced a good deal clinically by the localization of the lesions around the eyes, particularly the inner canthi.

DR. MARJORY K. HARDY: The patient has lesions on the lip and on the lobes of the ears. I think the swelling on the lower part of the nasal septum is interesting. I should like an opinion from some of the members as to what that may be.

DR. JOSEPH V. KLAUDER: I thought the lesions characteristic of what is particularly seen in tuberculosis in Negroes, the type of lesion around the nose and the lower eyelids. It is apparently a distinctive type of sarcoidosis in the Negro.

DR. MAX JESSNER (by invitation): I found the patient's condition extremely interesting as a combination of this sarcoid-like condition and the formation around the eyes. When I came here I was much astonished because I did not know this kind of case. I have studied this disease for ten or twelve years and collected a number of such cases in Breslau—about 120 in the last five years—but have not published them. When I came to the United States and saw all the tuberculids of the face, I preferred the nomenclature used in this country, because they all belong to the same group with a rather peculiar kind of immunity. There can be a negative reaction to tuberculin. It has always been a question where to classify these lesions, in the group of tuberculids or in the sarcoid group. I am convinced that they should be included in the sarcoid group because of this peculiar immunity.

Lupus Erythematosus Disseminatus. Presented by DR. MAURICE BROWN.

M. B., a Negress aged 24, presents an erythematous papular eruption in the butterfly area of the face, with occasional follicular plugging. She was in the hospital from June 29, 1941 to October 4 and was admitted with a history of headache, vertigo and ataxia for two weeks. Examination revealed the syndrome of thrombosis of the left inferior posterior cerebellar artery. The blood and the cerebrospinal fluid were normal. She was admitted again on March 23, 1942 with history of fever, weakness, malaise, photophobia, cough and occasional edema of the ankles since the previous admission. She had had no previous serious illness except diphtheria. She received an indefinite number of treatments for syphilis while in Georgia. She still has the neurologic indications of thrombosis of the left inferior posterior cerebellar artery. She also has a bilateral pleural effusion.

There is a persistent fever, with a temperature of 99 to 100 F. by mouth. Examination of the sputum and urine showed tubercle bacilli. The protein content of the blood was 6.1 Gm. per hundred cubic centimeters, with an albumin-globulin ratio of 1.0. The content of the urea nitrogen blood was 8 mg. and the sugar content was 104 mg. per hundred cubic centimeters. The Kline reaction of the blood was negative. A blood count showed 18,700 leukocytes, with 56 per cent polymorphonuclear leukocytes. Urinalysis revealed leukocytes and albumin. A roentgenogram of the chest showed bilateral pleural effusion and a small pericardial effusion.

DISCUSSION

DR. BERNARD L. KAHN: Within the past five years I have had a number of cases of lupus erythematosus disseminatus that terminated fatally. I should like to know whether any one can say what effect therapy with a sulfonamide compound would have on this disease.

DR. DONALD M. PILLSBURY: I have treated at least 10 patients with disseminate lupus erythematosus with various sulfonamide compounds. While at times they have seemed to have a temporary good effect, there was no permanent improvement from such therapy in my cases.

DR. FRED D. WEIDMAN: Hughes (ARCH. DERMAT. & SYPH. **42**:33 [July] 1940) reported good results.

DR. BERNARD L. KAHN: I read his article, and it inspired me to use sulfadiazine and sulfathiazole, but my patients did not improve under this therapy.

LOS ANGELES DERMATOLOGICAL SOCIETY

KENDAL FROST, M.D., *President*

ARTHUR FLETCHER HALL JR., M.D., *Secretary*

May 2, 1942

Leprosy (Lepromatous Type). Presented by DR. SAMUEL AYRES JR.

H. G., a 64 year old Mexican woman, has had lesions on her legs for seven months, several of the lesions having entirely healed. She noticed loss of her eyebrows eight or nine months ago. She has lived in Los Angeles for seven years, having lived in Mexico prior to that time. She has received injections in the legs for varicose veins and also some intravenous medication. The lesions are limited to the legs, which show irregular erythematous, necrotic and crusted nodular areas scattered over all aspects of the legs and ankles, especially the front and sides. On the anterior aspect of the right thigh are several slightly tender subcutaneous erythematous nodules. There are complete loss of eyebrows and slight thickening of the cheeks and nose. The skin of the arms is thin and atrophic. There is diminished pain sense in the hands and feet. Crusting is present on the nasal septum. A nasal smear showed many acid-fast bacilli, in packets, many with beaded appearance.

DISCUSSION

DR. IRVING BANCROFT: This case is somewhat similar to one which occurred here over ten years ago. A man had been selling fruit outside of the Los Angeles High School. It was five years before any one discovered he had leprosy.

DR. BEN A. NEWMAN: Does any one know how common leprosy is in Mexico?

DR. KENDAL FROST: I have heard it is very common there.

DR. CHRIS HALLORAN: The majority of the lepers seen in Los Angeles are Mexicans.

DR. H. C. L. LINDSAY: In Vancouver, British Columbia, Canada, I saw a man who sold tickets in a Japanese theater there. He was Japanese, and the day after his leprosy was discovered he went back to Japan, thus avoiding the health officers.

DR. HARRY JACOBSON: I remember the days when there was quite a colony of lepers here. I was interested in trying gold therapy.

DR. H. C. L. LINDSAY: It is interesting how leprosy will appear in isolated areas. I saw a Chinese girl who was raised near Vancouver who acquired anesthetic leprosy without known contact with it; none of her relatives had it.

DR. SAMUEL AYRES JR.: The patient has lived in Los Angeles about seven years. She has had the lesions about a year or less; so it is quite possible that she acquired the disease in Mexico. I doubt if much can be done outside of the health department's taking over, because the woman is without funds. I do not think it solves the question to let such patients go back to Mexico. It is not safe for the woman to be in any community.

Epithelioma of the Scalp. Presented by DR. ANKER K. JENSON.

E. M., a 79 year old white woman, states that her great-aunt had cancer of the scalp and her daughter had cancer of the uterus. Her present trouble began with a "mole" the size of a dime in 1917; it was electrodesiccated, but as the physician who had treated her went to war she did not have any more treatment for some time. Several years later she was given five roentgen treatments, which caused a "deep roentgen ray burn" and a piece of bone sloughed off. At that time there were two areas the size of a silver dollar. No treatment was given then for three or four years. After this period she had numerous cautery treatments and roentgen treatments, the dosages not known. The area is gradually spreading, but there is no pain associated with it. At present she is using boric acid ointment.

She now shows a palm-sized well marginated, rolled-bordered lesion on the top of the head. The lesion seems to be attached to the skull in places. It also presents a quarter-sized depressed area where the bone has sloughed out. The rest of the mass is ulcerative.

The Wassermann reaction of the blood was negative.

DISCUSSION

DR. SAMUEL AYRES JR.: There are some features that are suggestive of gumma to me. The border of the lesion looked a little doughy. I should not accept the diagnosis of epithelioma without further investigation, in spite of a negative reaction of the blood. I think one should perform a biopsy and investigate in regard to syphilitic possibilities.

DR. SAUL ROBINSON: I think that the lesion is an epithelioma, one of the reasons being that the nodule is in the scarred area. I think that if a biopsy is done of the nodule in the upper part of the lesion one will find epithelioma.

DR. ANKER K. JENSEN: I thought it would be interesting to see a patient who has suffered from epithelioma of the scalp for twenty-five years. I believe she illustrates the necessity for wide excision in the treatment of cancer. This lesion has been operated on many times and has been treated with roentgen radiation, but it has never been removed in toto. I am not going to advise any radical method of treatment, as she is almost 80 years of age and has had it so long.

A Case for Diagnosis (Mycosis Fungoides? Extracellular Cholesterosis?). Presented by DR. MAXIMILIAN E. OBERMAYER,

R. A., a 59 year old white woman, was presented before the New York Dermatological Society on Oct. 28, 1941 (ARCH. DERMAT. & SYPH. **45**:814 [April] 1942).

She has now sought advice because of an acute exacerbation of the disease, which developed shortly after her arrival in Southern California. The eruption consists of dull brownish, discoid, moderately infiltrated lesions at the sites mentioned in the previous record. Many of them were covered with scales and are psoriasiform, while some of them appeared vegetative and their surface exuded thin seropus. A specimen for biopsy was removed from one of the oozing lesions. Simple anti-inflammatory measures, such as the application of wet dressings of potassium permanganate (1:8,000) and a bland ointment, were sufficient to dry up the oozing lesions and to reduce their elevation to that of the other elements, thus proving that the first impression of vegetation was mistaken. The patient has been following a regimen of rest and relaxation and daily exposures to the sun with some improvement. The low cholesterol diet recommended by Dr. B. M. Kesten in New York is being continued. The histologic picture seems somewhat modified, compared to that illustrated and described from previous biopsies. The inflammatory infiltrate is more distinctly polymorphous, and the histiocytes are not as predominant.

Her blood count showed 5,180,000 erythrocytes and 13,450 leukocytes per cubic millimeter, with 72 per cent neutrophils, 24 per cent lymphocytes and 4 per cent large mononuclear leukocytes. The hemoglobin content was 15.64 Gm. per hundred cubic centimeters (92 per cent). The value for serum cholesterol was 190.5 mg. per hundred cubic centimeters.

DISCUSSION

DR. WILLIAM GOECKERMAN: I would, by exclusion, have to agree with the diagnosis as reported in New York.

DR. C. RUSSELL ANDERSON: My patient with "extracellular cholesterosis" died of lymphoblastoma. This patient's eruption looks like lymphoblastoma instead of reticulocytoma to me.

DR. NELSON PAUL ANDERSON: This patient presents an extraordinary picture. I am inclined to agree with Dr. C. Russell Anderson. First of all I do not believe that there is such an entity as extracellular cholesterosis. I feel that all of the patients who have been described as presenting this disease have had a special variety or type of lymphoblastoma. If one desires a more exact term, it can be called reticuloendothelioma or reticulocytoma. The high cholesterol content of the blood, which, incidentally, is not present in all cases, and the extracellular deposits of cholesterol in the skin are simply incidental to the process and not at all fundamental, as Urbach's term would indicate. One could make a number of new entities if every single disease of the skin were studied histologically by special stains for fat. As proof of the fundamental malignant or lymphoblastomatous character of this disease I would cite the fact that Urbach's patient had 9 per cent monocytes in the blood. C. R. Anderson's patient died of lymphoblastoma, and Layman's patient also died and no autopsy was permitted. I believe the outlook for the patient presented today is grave. That these patients all had the same variety of lymphoblastoma I am certain. One could take a photograph of Dr. Obermayer's patient and see its twin in a photograph of Dr. Urbach's, Dr. Anderson's or Dr. Layman's patient.

DR. C. RUSSELL ANDERSON: I did not know whether to call the eruption reticulocytoma or reticuloendothelioma. Interestingly, in the first case described by Urbach the eruption responded to roentgen rays at first, which seemed to prove it was some sort of blastoma. The clinical and histologic pictures are almost the same.

DR. WILLIAM GOECKERMAN: Dr. Nelson Paul Anderson's discussion has rather pointedly brought home thoughts I have had myself.

DR. H. C. L. LINDSAY: I do not think the disease is mycosis fungoides, because it has not responded well to roentgen rays.

DR. MAXIMILLIAN OBERMAYER: There is little to add to the extensive discussion before the New York Dermatological Society. I still believe that mycosis

fungoides should be taken into consideration, as the histologic picture is compatible with that diagnosis. However, as was pointed out by Dr. Lindsay, the absence of intense pruritus and the lack of response to roentgen treatments are difficult to reconcile with a prefungoid stage of that disease. I am not sufficiently acquainted with cholesterosis to have an independent opinion on that rare disease. Yet even if this diagnosis is accepted it does not explain the cause of the metabolic disturbance. The diagnosis of extracellular cholesterosis may be correct, but the process may constitute a forerunner to a lymphoblastoma, and I agree fully with the remarks of Drs. Nelson Paul and C. Russell Anderson. Perhaps it is worth mentioning that there is a functional and/or allergic element present in this case, which is evidenced by the presence of polyvalent dermal hypersensitivities to foods, dust, feathers, horse dander, timothy pollen and bacteria (staphylococcus), by the history of severe asthma and by certain features in her personality pattern. Whether or not this element has any etiologic connection with the present eruption I am unable to state.

CHICAGO DERMATOLOGICAL SOCIETY

Udo J. Wile, M.D., *President*

Michael H. Ebert, M.D., *Secretary*

May 20, 1942

A Case for Diagnosis (Nevus?). Presented by Dr. Marcus R. Caro.

C. B., a white girl aged 16, first had the present eruption at about 2 years of age. When she was examined in September 1938 there were lesions on all the present sites except for the left axilla. The patch there has developed since then. At first there was severe itching and the patient scratched a good deal, but the eruption is free from symptoms now. No pathologic changes were disclosed by a general physical examination. The Mantoux test with a dilution of 1:1,000 gave a negative result.

The cutaneous lesions are of two types. In the right axilla and on the inner surface of both arms below the axillas are circumscribed patches of lichenified dermatitis. On the inner surface of the left thigh are patches of lichenified dermatitis with outlying small follicular papules. Across the lower part of the abdomen is a poorly outlined wide horizontal band composed of closely aggregated pinhead-sized translucent brownish red papules, which give the area a cobblestone appearance.

Biopsy of a specimen of skin taken from the abdomen, a papule about a hair follicle, showed a slight edema of the epidermis and papillae. The chief pathologic change was a sharply circumscribed mass of cellular infiltrate in the subpapillary portion of the corium. This was composed of lymphocytes with many epithelioid cells and a few giant cells. There was also a mantle of these cells extending down along the hair follicle. Elastic fibers were absent in the areas of infiltration. Staining for lipids, amyloid and acid-fast bacilli gave negative results. A slight amount of iron pigment was demonstrated within a few of the cells.

DISCUSSION

Dr. Otto H. Foerster, Milwaukee: This patient had axillary lesions which are recent. I think the condition is nevoid.

Dr. S. W. Becker: The color of the lesions suggests cutaneous amyloidosis. The histologic sections show a dermal infiltrate which is somewhat tuberculoid in structure and suggests atypical sarcoid. I have never seen anything like it clinically, and the microscopic picture is also unusual.

DR. THEODORE CORNBLEET: I thought of congenital ichthyosiform erythroderma. The eruption is dry, scaly and erythematous and favors the flexor surfaces. The lesions on the abdomen are not unlike some I have seen in cases of congenital ichthyosiform erythroderma.

DR. CARL W. LAYMON, Minneapolis: After looking at the histologic sections, Dr. Winer felt that this patient might have atypical pityriasis rubra pilaris.

DR. MARCUS R. CARO: I cannot make a definite diagnosis in this case. When I first saw the histologic sections I was struck with the tuberculoid structure. The Mantoux reaction, however, was negative, and roentgenograms and the physical examination of the chest failed to reveal evidence of tuberculosis. The clinical and the histologic appearance has remained unchanged during the several years that I have observed the patient. I think that the diagnosis will prove to be a nevoid structure.

Pseudoxanthoma Elasticum with Angioid Streaks. Presented by DR. HERBERT RATTNER and DR. MAURICE DORNE.

Mrs. E. W., a Negress aged 51, was admitted to the ophthalmic department of the Cook County Hospital because of a progressive deterioration of vision for the past four years. Angioid streaks were noted in the retinas. She did not complain of cutaneous symptoms. She had been receiving antisyphilitic treatment in the City Health Department Clinic since 1937. Her past history is irrelevant.

She presents poorly defined striate lesions, situated symmetrically on the sides of the neck. When stretched the patches assume a yellowish tinge. The patches have a crinkly surface, giving the appearance of atrophy.

A roentgenogram of the chest was reported as normal. The blood and urine were normal, and the Kahn reaction was negative.

DISCUSSION

DR. OTTO H. FOERSTER, Milwaukee: This is the first time I have seen this disease in a Negro.

DR. CLARK W. FINNERUD: I think this is the first time I have seen the disease in a Negro. In the majority of cases reported in the past the eyegrounds have not been examined thoroughly. It has been shown in the last two or three years that pseudoxanthoma elasticum is commonly associated with angioid streaks of the retina. I did not see the histologic sections, but the condition is always easily diagnosed histologically.

DR. HERBERT RATTNER: It is interesting to note that this patient was sent to us from the ophthalmic department with the inquiry as to whether the lesion on the neck was pseudoxanthoma elasticum. I have not yet had an opportunity to go over the hospital records to determine whether there has been a similar condition in another Negro.

A Case for Diagnosis. Presented by DR. HERBERT RATTNER and DR. MAURICE DORNE.

Mrs. C. C., a Negress aged 41, a decipara, having been gravid thirteen times, states that in March 1942 she sustained a number of burns on her right hand, forearm and arm from a hot iron. She applied various home remedies, but the original lesions became infected and progressively larger and a number of new, smaller lesions developed in the area.

The past history is irrelevant except for gonorrhea in 1930.

The lesions are present only on the right hand, forearm and arm. They vary in size from that of a pea to that of a silver dollar and are arranged in sharply circumscribed, irregularly circinate patches. In places the polycyclic outline is sharp. The lesions are purplish and covered by a dry scale which is somewhat adherent. The small ones are lichenoid.

The urine was normal.

DISCUSSION

DR. LEONARD F. WEBER: I think the patient has a dermatitis factitia.

DR. S. W. BECKER: I do not know what this disease is called clinically, but the histologic sections showed a pronounced round cell infiltration and I thought of some form of lymphoblastoma.

DR. RUBEN NOMLAND, Iowa City: I thought of a pyogenic infection of the skin. I do not believe the patient could produce lesions such as she has. I think there is a constitutional background. Occasionally such an eruption is seen in a chronic ulcerative colitis.

DR. HERBERT RATTNER: We saw this patient for the first time last week, and at first we thought that the lesion was an unusual type of syphilis. Some of the lesions also suggested lichen planus.

Lupus Erythematosus. Presented by DR. HERBERT RATTNER and DR. MAURICE DORNE.

M. F., a white woman aged 44, states that four months ago an eruption of pinhead-sized nonitching pimples developed on the nape of the neck following a treatment of the scalp for falling hair. Two and a half months later lesions appeared on the chest, and in the past four weeks lesions have made their appearance on the forearms, hands and face. Arthritis affecting the fingers, which is still present, was first noted one month after the appearance of the first cutaneous lesions.

On the scalp there is a sparse eruption of thickened papules covered with scales. Scale-covered erythematous papules are present on the inner canthus of the right eye, on the anterior rims of the ears and on the nose. There are also some lesions on the left side of the hard palate. On the V of the chest, the upper part of the back, the extensor surfaces of the forearms and the dorsa of the fingers, there are large erythematous patches covered with scales. The patches have a serpiginous outline. There are also telangiectatic lesions on the fingers. There is no detectable cardiac lesion. Her temperature has been fluctuating and has reached 101 F. on several occasions.

Examination of the blood showed 59 per cent hemoglobin, 3,090,000 erythrocytes and 6,000 leukocytes, with a differential count of 59 per cent neutrophils, 36 per cent lymphocytes and 5 per cent monocytes.

A roentgenogram of the chest was reported as normal. Urinalysis revealed a trace of albumin, a few pus cells and a few granular casts.

Lupus Erythematosus Disseminatus. Presented by DR. D. V. OMENS, DR. H. D. OMENS (by invitation) and DR. A. FALK (by invitation).

E. B., a white girl aged 15, noticed a flush on her cheeks one month ago and three weeks later a rash on her arms and legs.

There is an erythema of the face which is most evident in the central oval and extends over the nose and cheeks. A fine tenacious scale is present, as is some follicular dilatation in the aforementioned zones. A sparse eruption is present on the hands and knees, composed of split pea–sized lesions which are maculopapular. A small lesion is present on the hard palate. At present she has a low grade fever. This is the sixth seasonal exacerbation that the patient has experienced.

For the past five years she has used Vick's nose drops (a mixture of menthol, camphor, eucalyptus and other aromatics, with a small amount of ephedrine, in a liquid petrolatum base) daily. Examination of the nose shows bulging of the septum. A submucous resection was advised when the patient is older.

Roentgenograms of the chest and paranasal sinuses were normal. Chemical determinations on the blood gave normal results. Wassermann and Kahn reactions were negative. The hemoglobin content was 64 per cent. There were 3,750,000 erythrocytes and 3,400 leukocytes, with 50 per cent polymorphonuclear neutrophils,

1 per cent eosinophils, 40 per cent lymphocytes and 7 per cent monocytes. The urine was normal.

DISCUSSION OF CASES OF LUPUS ERYTHEMATOSUS

DR. RUBEN NOMLAND, Iowa City: I could not agree with the diagnosis of lupus erythematosus in Dr. Rattner's case. I thought it was pemphigus erythematodes, although the histologic sections were more suggestive of lupus erythematosus.

DR. FRANCIS E. SENEAR: I thought of the possibility of pemphigus erythematosus also in this case. The factors which would rule out such a diagnosis are the extensive involvement of the dorsal surfaces of the hands and forearms, where one does not ordinarily see pemphigus erythematosus, and the picture as a whole. I thought some of the lesions were suggestive of bullae undergoing involution in an acute stage, but there was no suggestion of the formation of a hyperkeratotic type of lesion which is characteristic of that disease. However, the histologic picture can so definitely differentiate lupus erythematosus disseminatus and pemphigus erythematosus that if the histologyic sections in this case favor the diagnosis of lupus erythematosus I would accept it.

DR. OLIVER S. ORMSBY: There has been some controversy about pemphigus erythematosus. Some of the eastern colleagues state that the disease which has been seen here has been lupus erythematosus with bullae and that pemphigus erythematosus is not an entity. This patient has the type which is lupus erythematosus with bullae.

DR. HERBERT RATTNER: I saw this patient for the first time last week. The eruption suggested pemphigus, but because of the telangiectatic lesions on the fingers the diagnosis of lupus erythematosus was finally decided on. I believe that both these patients present anomalies in some respects. The condition of my patient is of only a few weeks' duration, yet is rapidly getting worse, whereas the other patient with the erythematoid type of eruption is doing well with no other treatment than rest in bed.

Pemphigus Vulgaris. Presented by DR. EDWARD A. OLIVER.

J. H., a woman aged 55, states that her first cutaneous symptoms began in 1937 with lesions in the mouth, which she thought were gum boils. In July 1938 lesions began to appear on the skin of the face, neck and chest. In 1938 she was admitted to the Cook County Hospital, where she remained for five and one-half months. She was discharged on Aug. 25, 1939, after having received considerable treatment with a great deal of benefit. She had been almost entirely free of symptoms until several weeks ago, when the present eruption began.

DISCUSSION

DR. MAURICE OPPENHEIM (by invitation): This patient shows the lesions of pemphigus vulgaris. Dr. Oliver told me that the patient first noticed lesions in the mouth in 1937 and that a general rash appeared on the skin one year later. The incubation period in cases of this kind, that is, the time between the primary lesion and the outbreak on the skin, may be from six weeks to many months or even a year. I suggest that in all cases in which there is a primary lesion in the mouth or on the scalp or in some other area, treatment should be started immediately if pemphigus is suspected. The primary lesions do not heal with common treatment, and this fact is the first to suggest the development of pemphigus later. I suggest that acetarsone be given immediately.

DR. STEPHEN ROTHMAN (by invitation): I should like to ask about the differential diagnosis from dermatitis herpetiformis because of the polymorphism of the lesions.

DR. THEODORE CORNBLEET: I believe that erythema multiforme must also be considered; I feel, though, that it is impossible to make a definite diagnosis right now.

DR. PAUL A. O'LEARY, Rochester, Minn.: A year ago at a meeting of this society I suggested that pemphigus is running a milder course or that dermatitis herpetiformis is assuming more severe features. This patient seems to illustrate the point. For several years I have seen with increasing frequency patients who present bullous lesions of the mucous membranes, with bullous cutaneous eruptions developing later and with the disease settling down in a short time to follow a prolonged, benign course. At present I consider that these patients have dermatitis herpetiformis, because of the benignity of the disease, in contrast to the virulence of pemphigus. If this is so, lesions on the mucous membranes are not now uncommon in dermatitis herpetiformis. In any event, I am having more trouble in differentiating these two diseases.

DR. MICHAEL H. EBERT: During the last few years I have observed a number of cases such as Dr. O'Leary has described in which on physical examination and frequently on many subsequent examinations the picture was extremely suggestive of dermatitis herpetiformis; there were a multiplicity of lesions and subjective manifestations in the form of burning and itching; there were few lesions in the mouth, and months might go by without their appearance. The eosinophil count was usually high, and the condition certainly resembled severe dermatitis herpetiformis. However, I do believe that when this disease occurs in persons in their fifties or sixties it will eventually end in a fatal pemphigus. I should be surprised if this does not happen in this case. This patient was in the hospital some months ago, and blood transfusions seemed to have a beneficial effect. At present I suggest high doses of vitamin D. I know that as therapy for pemphigus this has not been a panacea, but I have a case in mind in which the disease was similar to this but more severe and it looked as though the patient had a very short time to live. She responded rather miraculously to the administration of vitamin D, and that response has continued for six months. I think that in such cases this treatment should be given a trial, but it would also be well to remember the possibility of toxic reactions from its use.

DR. PAUL A. O'LEARY, Rochester, Minn.: Perhaps the use of sulfapyridine might be a therapeutic test, in view of the fact that results in dermatitis herpetiformis at the clinic have been rather encouraging.

DR. HERBERT RATTNER: About three years ago this woman was treated with rabies vaccine, after which the lesions disappeared. It was found, however, that in the case in which the disease was not fatal there was always a difference of opinion as to whether or not the condition was pemphigus. When there was complete agreement on the diagnosis of pemphigus, the course was fatal.

DR. E. A. OLIVER: Three years ago I referred this patient to the dermatologic service of the Cook County Hospital, and under treatment there she has improved a great deal. She has had very little trouble until just recently. Today she presents a rather extensive eruption on the body together with many lesions on the mucous membranes. This case illustrates the fact that many of these patients go on for three to four years having remissions and exacerbations. They finally succumb to the disease, however. I believe the prognosis in this case is serious.

Urticaria Pigmentosa. Presented by DR. DAVID V. OMENS, DR. HAROLD D. OMENS (by invitation) and DR. CHARLES E. KEMP (by invitation).

J. L., a girl aged 4 years, presents a pigmented macular eruption involving the forehead, back and abdomen, which has been present for one year. There are no subjective symptoms, but on being stroked the lesions urticate. The child is one of three siblings. The first, 12 years old, has had recurrences of hives for several years; the youngest, 5 months old, has no illness. There is no familial history on either side of an allergic state, except in the oldest child.

The patient was seen for the first time in the clinic this morning.

Lupus Vulgaris with Pulmonary Tuberculosis. Presented by Dr. E. A. Oliver and Dr. S. M. Bluefarb (by invitation).

N. S., an American woman aged 24, was presented at the March meeting of this society (Arch. Dermat. & Syph. **46**:600 [Oct.] 1942), at which time it was suggested that arsenical therapy be tried. Since the last presentation she has had four intravenous injections of mapharsen at the Winfield Sanatorium, Winfield, Ill., without any improvement in her cutaneous lesions. She has been discharged from the sanatorium. There has been much improvement in her pulmonary lesion but little, if any, in her cutaneous lesions.

DISCUSSION

Dr. E. A. Oliver: Some of the members wanted this case brought up again for discussion. Three weeks ago I sent histologic sections, colored pictures and black and white photographs of this patient to Dr. Michelson to get his impression of the case. He replied that in view of the fact that the patient had not been helped by any of the local therapy used so far he felt that any further local treatment would be of no value. He suggested that a strictly salt-free diet be employed and that if she did not respond to this roentgen treatment be used. Another form of treatment that I am considering is desensitization through inhalation of broth cultures of tubercle bacilli. This method of treatment has been used by several internists with excellent results in cases of tuberculous iritis. It is still in an experimental stage, but I believe it is worth trying.

Dr. Theodore Cornbleet: Dr. S. R. Rosenthal and I have been conducting immunologic and therapeutic experiments in tuberculosis of the skin of diverse types in which we used BCG vaccine. The material is administered by inhalations in a vaporized state. The results are encouraging. I should like to recommend this type of treatment.

Dr. Stephen Rothman (by invitation): I do not agree with the statement that external treatment would not help in removing the crusts and scales. Such a condition is often seen in neglected cases of lupus vulgaris with ulcerations. The skin can easily be cleansed by applications of mild salicylic acid ointments and wet dressings. Mild local and general ultraviolet irradiation should be started immediately after such cleansing. This girl was treated for three or four months with intensive irradiation with a Finsen lamp, and the eruption spread.

Dr. E. A. Oliver: The debris and crusts were removed and mild antiseptic ointments were applied, but the eruption has continued to spread.

A Case for Diagnosis (Pityriasis Lichenoides Chronica?). Presented by Dr. E. A. Oliver and Dr. A. R. Koransky (by invitation).

T. B., a white girl aged 16, was admitted to the allergy clinic of Northwestern University in August 1940, for treatment of asthmatic attacks which have persisted for the past four years. During treatment for her asthma in the clinic she had a cutaneous eruption which has been present for the past year. This eruption involves the neck, trunk, arms and legs. In some areas where the lesions have cleared loss of pigment is seen. Itching is present to a moderate degree.

Her past history reveals that she had eczema as an infant. She has also had occasional attacks of urticaria.

Examination of the blood on May 13, 1942 revealed hemoglobin 12.8 Gm. per hundred cubic centimeters, erythrocytes 5,310,000 and leukocytes 9,200, with a differential reading of 55 per cent polymorphonuclear neutrophils, 15 per cent eosinophils, 25 per cent lymphocytes and 5 per cent monocytes. The urine was normal.

DISCUSSION

Dr. Paul A. O'Leary, Rochester, Minn.: The diagnosis of pityriasis lichenoides chronica seems warranted.

DR. FRANCIS E. SENEAR: I also think this patient has pityriasis lichenoides chronica, but there are certain factors to consider. The lesions are rather acutely inflammatory in places and suggest those of the Haberman type. I have observed several instances in which the acute varicelliform variety has gradually quieted and changed to become a typical Juliusberg type. Some of the lesions in this case were excoriated, but she says that she scratches, so some of these lesions which have broken down may not have done so spontaneously. Nevertheless, I feel that one should definitely consider the possibility that this eruption had begun as the acute type of parapsoriasis.

DR. STEPHEN ROTHMAN (by invitation): I agree with the diagnosis of pityriasis lichenoides chronica.

DR. MAURICE OPPENHEIM (by invitation): I agree with the diagnosis of pityriasis lichenoides chronica, but the eruption resembles the variety of pityriasis lichenoides varicelliformis because some of the lesions show a central necrosis. This form often heals with a leukoderma. Another deciding factor would be a Mantoux test. In the majority of such cases the Mantoux and Pirquet reactions are strongly positive.

DR. OTTO H. FOERSTER, Milwaukee: The presence of leukoderma can be regarded as confirmatory evidence in such cases, for it occurs with unusual frequency in pityriasis lichenoides chronica. This girl shows evenly distributed dark pigmentation, and when she is examined closely a leukoderma is seen along the sides of the neck and on the shoulders.

DR. E. A. OLIVER: I felt that this patient had pityriasis lichenoides chronica. When I first saw her I thought she might have pityriasis lichenoides et varioliformis acuta, but I have never seen any vesicles or any hemorrhagic crusts. I think the condition should be put in the chronic group.

A Case for Diagnosis (Idiopathic Atrophy?). Presented by DR. EDMUND N. WALSH (by invitation).

This patient, a Hungarian and Rumanian steel worker aged 26, has noticed a change in the color of the skin of the right arm and of the legs for the past year. The change seemed to start on the right elbow in a scar from a boil he had had several years ago. The disease has gradually spread to its present extent. About three months ago he first noticed changes in the skin of the feet, limited to the shoe area. Since then similar spots have appeared on the leg and thigh. There are no subjective symptoms.

The patient is American born but returned to Rumania at the age of 5 years. He came back to America at the age of 21. He was working in a poultry shop at the time the lesions appeared. There is no history of serious illness and no family history of a similar disease.

Physical examination shows no abnormalities except for a large scar from a burn on the left side of the abdomen and the cutaneous changes mentioned.

The Wassermann reaction was negative. The blood was normal.

Histologic examination showed the following changes. The epidermis was flattened. Throughout the corium there were sharply outlined nests of cells about the smaller blood vessels. These contained densely packed, uniformly small cells containing a large deeply staining nucleus. Elastic fibers were present throughout the corium but were fragmented in the upper part.

DISCUSSION

DR. S. W. BECKER: I had a chance to see this patient some weeks ago, and at that time there was some suggestion of morphea. However, the lilac border could not be identified. There seemed to be distinct atrophy. This man was born in this country but was taken to southern Europe as a child and spent most of his life over there, where idiopathic atrophy is seen more frequently than here. I should be inclined to diagnose this eruption as idiopathic atrophy.

DR. CLARK W. FINNERUD: I think this case is extremely atypical if the condition is idiopathic atrophy. My first impression was of morphea, but after examining the patient more closely I believe he has the so-called idiopathic atrophy.

DR. STEPHEN ROTHMAN (by invitation): The sharp borders of the atrophy on the upper parts of the arms are unusual, but all other clinical signs are rather characteristic for acrodermatitis chronica atrophicans. Particularly characteristic are the atrophy of the elbow and the "ulnar stripe" of Herxheimer.

DR. MARCUS R. CARO: I think that idiopathic atrophy can be ruled out on the histologic section, but I cannot offer another diagnosis.

DR. MAURICE OPPENHEIM (by invitation): Another diagnosis which might be considered is acrodermatitis chronica atrophicans of the ankle with some pseudosclerotic changes. Parts of the skin are stiff and inelastic. The stripe over the ulnar bone might be the beginning of the same condition on this location. I must admit the sharp margin of the lesion is unusual for acrodermatitis chronica atrophicans.

Naevus Araneus Type of Telangiectases with Cirrhosis of the Liver. Presented by DR. EDMUND N. WALSH (by invitation).

This 50 year old Jugoslav steel worker has noticed red spots on the face for the past year. More recently they have appeared on the arms and upper part of the chest. There are no subjective symptoms.

The patient gives a history of moderate to heavy alcoholic intake for many years. About two years ago he began to have abdominal distress after drinking. Two months ago he stopped drinking entirely. The spots seemed to have improved slightly, and no new ones have appeared. He has gained 5 pounds (2.3 Kg.) in weight.

An examination in December 1941 showed a normal blood count, a negative Wassermann reaction and normal roentgenograms of the stomach. A diagnosis of cirrhosis of the liver was made at that time. At present the liver is firm and smooth and extends about 5 cm. below the costal margin.

DISCUSSION

DR. PAUL A. O'LEARY, Rochester, Minn.: I believe Dr. Williams and Dr. Snell (Pulsating Angioma [Generalized Telangiectasis] of the Skin Associated with Hepatic Disease, *Arch. Int. Med.* **62**:872-882 [Nov.] 1938) first called attention to the significance of "pulsating nevi." Their patient had definite pulsations in the nevi which could be elicited by applying light pressure with the diascope. The significance of these lesions is that they are associated with early cirrhosis of the liver.

DR. S. W. BECKER: Dr. Walsh and I published a series of cases of naevus-araneus-like lesions in pregnancy. Histologic sections showed that the lesions consisted of central arteriovenous connections, which probably account for the pulsation.

Pigmented Purpuric Lichenoid Dermatitis of Gougerot and Blum. Presented by DR. HERBERT RATTNER and DR. A. FALK (by invitation).

A. B., a white man aged 23, first noticed a brownish eruption of the skin on his ankles two years ago. The eruption caused him no difficulty, but since it did not disappear he decided to have medical consultation.

Examination shows grouped papular lesions located anteriorly and posteriorly to the external malleoli of both ankles. These lesions are brown and have a fine scale. On diascopic pressure fine pinpoint-sized hemorrhages are seen.

DISCUSSION

DR. CARL W. LAYMON, Minneapolis: This dermatosis has always been a source of great confusion to me, especially as to its differentiation from Scham-

berg's disease. When the condition was first described, the presence of small papules was stressed as an important differential point. Later the French investigators and others who have observed these cases came to believe that both pigmented purpuric lichenoid dermatitis of Gougerot and Blum and Schamberg's disease are but odd forms of stasis dermatitis.

DR. MARCUS R. CARO: I had one other thought about this case histologically, and that is that the eruption might be an unusual form of lichen planus. The sharply circumscribed infiltrate in the upper part of the corium suggested this, even though the changes of acanthosis and thickening of the granular layer were not present.

DR. HERBERT RATTNER: For some time I have been looking for a case of this disease, and this is the first one that I thought might fit the description. In 1935 Wise reported the first case from this country and made the point that a distinguishing characteristic is that the individual papules do not enlarge peripherally. In lichen planus there may be patches and in Schamberg's disease there are defined papules. There has always been the question as to whether this condition is an entity. Certainly the clinical features present early in its course, as in this case, are distinctive.

Juxta-Articular Nodes. Presented by DR. MAURICE OPPENHEIM (by invitation) and DR. D. COHEN (by invitation).

L. B., a white man aged 63, presents on both hands and fingers tumors ranging in size from that of a bean to that of a hazelnut. On the left forearm near the elbow there is a large cystic mass the size of a hen's egg. Many of the tumors are hard and globelike, while others show fluctuation and some have lobular structure like lipomas. Some of these lesions are motile, and others are fixed to the overlying skin.

Both hands show advanced arthritis deformans. There are scars on the hands and feet following surgical treatment. He has had chronic arthritis for twenty-three years. He is known to have syphilis, having had treatment at various intervals.

The blood and urine were normal. The Kahn reaction was positive.

DISCUSSION

DR. MAURICE OPPENHEIM (by invitation): The patient has not only syphilis but arthritis deformans. As for the juxta-articular nodes, most authorities believe that they are caused by Spirochaeta pallida. Hopkins and others believe they find the juxta-articular nodes in arthritis deformans too. However, S. pallida has been found in cases of this disease, and the lesions disappear often under antisyphilic treatment. Both of these statements would tend to prove that S. pallida is the causative factor. It is my belief that these nodes not only are caused by syphilis but can be caused by arthritis deformans too. I feel sorry that this remarkable case with regard to the cause of the juxta-articular nodosities was not discussed by those present.

A Case for Diagnosis (Pustular Psoriasis?). Presented by DR. MICHAEL H. EBERT.

J. W., a white man aged 36, had arthritic pains in his left knee associated with swelling six weeks ago. The electric pad was used constantly. Four weeks ago numerous split pea–sized vesicles developed in this area, and a week later his nails started to become separated distally and distorted, both finger and toe nails being involved. A few dry scaly lesions appeared on the penis. The vesicles dried leaving a thickened, rupioid scale. When this was removed a moist surface was exposed.

The patient gives a history of having had repeated attacks of gonorrheal arthritis during the last seven years. Repeated examinations of the smears from the prostate and seminal vesicles disclosed no gonococci. The result of a com-

plement fixation test for gonococci was negative in this laboratory and in an outside laboratory. A blood count and chemical examination of the blood disclosed nothing of significance. Wassermann and Kahn reactions of the blood serum were negative.

Biopsy of an early lesion showed a thickened stratum corneum made up of lamellas which were separated in many places by accumulations of round cells. The epidermis was edematous and acanthotic. The papillae approached close to the surface. The edema in the upper part of the rete was great in places, and small microabscesses were found to contain many round cells. There was extensive migration of leukocytes through the acanthotic rete. There was moderate round cell infiltration in the papillary and subpapillary layers of the corium.

DISCUSSION

DR. FRANCIS E. SENEAR: It is opportune for the members to observe this case today after the discussion of last month concerning the man whose condition could not be agreed on. Dr. Mitchell said that the involvement of the nails could not be used as a differential point between pustular psoriasis and acrodermatitis continua, since the nails were affected in both diseases. I think that the changes in the nails shown here today were unquestionably those of psoriasis and not the type seen in acrodermatitis continua.

I was particularly interested in this case because of the lesions on the knee. Dr. Shellow was examining the patient and called attention to the fact that when the scales were removed there was no apparent change in the skin beneath them. On Tuesday I saw a patient at the University who had arthritis and also what I felt was a pustular psoriasis with involvement similar to that in this case. He had lesions on the legs which had the characteristic thick scale, and when those were lifted off—much to my surprise—the skin underneath appeared to be normal. That patient gave a history of an old gonorrheal infection, and many of the lesions on the under surface of the toes made me think of the possibility of keratosis blennorrhagica, in that case as well as in this one, but the changes in the nails in that case were not present as they are in the case shown today.

DR. CLARK W. FINNERUD: I questioned this patient about gonorrhea, and he stated that he had an original infection in 1927 and has had frequent recurrences up to the present. The lesions even in gonorrheal keratoses can be vesicular, pustular or even bullous in the beginning if the process is acute. I think that with the articular manifestations, the lesions that are present and the history, the chances are that this patient has gonorrheal keratosis rather than psoriasis.

DR. RUBEN NOMLAND, Iowa City: I should like to agree with Dr. Finnerud. I am inclined to believe that the patient has a gonorrheal keratosis associated with gonorrheal rheumatism. Such a rheumatism responds well to induced fever, while psoriasis does not respond as rapidly.

DR. PAUL A. O'LEARY, Rochester, Minn.: Another point in favor of the diagnosis of psoriasis is the arthritis. The only distinguishing feature between infectious and psoriatic arthritis is the onset of the latter in the terminal phalanges. My own experiences tend to parallel those already expressed here, but I have come to attach great significance to the development of arthritis in the terminal phalanges in a patient with psoriasis. It is well to emphasize the fact that arthritis occurs in certain patients with psoriasis in which the diseases are unrelated and also that when it does occur psoriatic arthritis in my opinion is a definite entity.

DR. MICHAEL H. EBERT: The only disease that offers a pathologic picture analogous to that of psoriasis is keratosis blennorrhagica. If one did not know the history in this case and only saw the sections, one would think the patient had pustular psoriasis. There is a close resemblance between these two diseases. Keratosis blennorrhagica is produced by infection, and it has made me feel that one might find some source of infection to produce the lesions of psoriasis.

DR. EARLE R. PACE: May I add one thing about changes in the nails? I had a case of well substantiated gonorrheal dermatitis in which the nails of all the

toes and of four of the fingers were lost. There were changes all the way from mild opacities to pustular mutilation.

A Case for Diagnosis (Lymphoblastoma?). Presented by DR. MICHAEL H. EBERT.

P. R., a Mexican aged 20, first noticed a "tumor" on his left leg in March 1941. A biopsy was performed at another clinic, and the diagnosis was fibrosarcoma. In December 1941 purpuric streaks developed on the body, which apparently occurred spontaneously. Within the past six weeks infiltrated plaques have appeared on his cheeks.

At present a bluish red, raised, moderately infiltrated plaque occupies the upper half of each cheek. There are numerous linear streaks on the chest and sides of the trunk made up of hemorrhages. There appears to be some atrophy of the interosseous muscles of the right hand.

The Wassermann and Kahn reactions were negative. The erythrocyte count was 2,850,000 and the leukocyte count 4,250, with 19 per cent polymorphonuclear neutrophils, 42 per cent lymphocytes, 2 per cent monocytes and 36 per cent immature forms.

A nasal smear and smears of serum from the lesions failed to reveal lepra bacilli. No lepra bacilli were found in sections made from the lesions on the cheeks.

A biopsy showed that the corium was infiltrated with a large number of immature cells of the lymphocyte type.

NOTE.—Shortly after the meeting the patient had a high temperature, and within two weeks the plaques on the face were absorbed completely. He rapidly lost weight and strength, and in spite of repeated blood transfusions he died four weeks after the meeting. At no time was there a leukemic blood picture.

DISCUSSION

DR. MICHAEL H. EBERT: I never saw this patient until this afternoon. He has been studied in other departments of the hospital. So far as the diagnosis is concerned, the field is open.

DR. OTTO H. FOERSTER, Milwaukee: The nodular masses on the cheeks and elsewhere and the presence of muscular atrophy, without mention of the other changes present, lead one to a diagnosis of leprosy.

DR. FRED T. BECKER (by invitation), Duluth, Minn.: I also thought of leprosy. The patient had large, tender ulnar nerves and typical atrophy of the interosseous muscles.

DR. LOUIE WINER (by invitation), Minneapolis: Noticeable was the anesthesia of the infiltrated plaques and the hyperesthesia in other parts. I think all the facts mentioned plus these lead one to suspect leprosy.

DR. JAMES H. MITCHELL: I agree with a diagnosis of leprosy.

MAJOR SAMUEL GOLDBLATT (by invitation), Fort Sheridan, Ill.: I also agree with the diagnosis of leprosy. The only thing that puzzles me is the presence of purpuric streaks. I have never seen these in any other disease, and I do not know that it occurs in leprosy either.

DR. RUBEN NOMLAND, Iowa City: I should like to agree with the presenter that this patient has lymphoblastoma which is relatively acute. I believe the blood picture is sufficient to establish the diagnosis. The patient has a profound anemia. Before one makes a diagnosis of leprosy there should be proof of such a diagnosis.

DR. MARCUS R. CARO: The Wassermann reaction was negative, and the red blood cell count was 2,850,000.

DR. MICHAEL H. EBERT: Of course, this case should have been presented for diagnosis. The histologic sections should settle the question of lymphoblastoma.

Small Papular Tuberculid. Presented by DR. A. W. STILLIANS.

A Negro boy aged 9 years was discovered to have tuberculosis of the left lung during an examination at school two years ago. His sputum was free from tubercle bacilli at this time and has been free since. The reaction to a Mantoux test was positive with old tuberculin in a dilution of 1 : 10,000. At the time he entered the Municipal Tuberculosis Sanatorium two years ago he had phlyctenular conjunctivitis and clubbed fingers. Wassermann and Kahn reactions were negative. The urine was normal. Examination of the blood showed 70 per cent hemoglobin, 4,580,000 erytherocytes and 7,550 leukocytes, with a differential count of 62 per cent neutrophils, 5 per cent eosinophils, 1 per cent basophils, 6 per cent stab cells, 56 per cent segmented forms, 22 per cent small lymphocytes, 5 per cent large lymphocytes and 5 per cent monocytes.

In January 1942 an eruption of small papules, 1 to 3 mm. in diameter and sharply elevated, 1 to 2 mm., lighter brown than his skin, was noticed on the face, ears, chest and upper part of the back. Some of these papules had a central depression, suggesting molluscum contagiosum, but lacked the pearly hue and yielded nothing except blood on puncture. This eruption is now resolving, leaving depigmented spots. No ulceration has been seen in any of the lesions.

A section of one of the papules on the back showed acanthosis and fusion of the interpapillary pegs, with many cells in the basal and prickle cell layers represented by a pyknotic nucleus in the center or at the side of an empty space. In places the prickle cells were pressed together, elongated into bands, with a clear space on each side of the nucleus. The intercellular bridges were visible at the sides of these bands. In the upper part of the corium there were much edema and a moderate amount of round cell infiltrate. In the reticular layer there were small masses of infiltrate in a loose network of connective tissue. In the center of the larger of these were two foci of necrosis.

Rosacea-Like Tuberculid. Presented by DR. A. W. STILLIANS.

An American woman aged 24 was shown with the first attack of this disease at one of the meetings of this society in 1939 (ARCH. DERMAT. & SYPH. **41**:1165 [June] 1940). Her pulmonary infection was discovered in the winter of 1937-1938. When she entered the Municipal Tuberculosis Sanatorium, in March 1938, her sputum contained tubercle bacilli. In January 1939 the sputum was free from bacilli, and the next month the eruption began on the face. At that time the reaction to a Mantoux test was positive with old tuberculin in a dilution of 1 : 10,000. Her eruption cleared under treatment with roentgen rays (eleven treatments) in May 1940 but recurred last November. There are no signs of a pulmonary recurrence. She is on a modified Gerson diet.

The present eruption is not as extensive as was the first one. It involves the cheeks and is composed of minute yellowish red papules, thickly aggregated but discrete on the cheeks near the nose, becoming less numerous on the outer parts of the cheeks. The color of these papules is yellowish red, varying from time to time according to the amount of congestion and at times nearly disappearing.

Lichen Scrofulosorum Associated with Phlyctenular Keratitis. Presented by DR. MICHAEL H. EBERT.

E. C., a Negress aged 8 years, presents a generalized cutaneous eruption of five weeks' duration and a lesion of the left cornea of ten days' duration. The personal and family histories are not significant. The child has lost no weight and has had no chronic cough or night sweats.

On examination she presents numerous minute follicular papules. On the face and ears and neck these are discrete. On the trunk and extremities they tend to be grouped and have a faint scale.

The reaction to a Mantoux test was strongly positive with a dilution of 1 : 100,000. The Wassermann and Kahn reactions of the blood serum were nega-

tive. There were 4,600,000 erythrocytes and 12,000 leukocytes, and the differential count was normal. A roentgenogram of the chest showed a widening of the mediastinal shadow suggesting a probable lymphadenopathy. It was the opinion of the roentgenologist that the findings suggested a primary phase of tuberculosis. The ophthalmic department reported that the patient was suffering from a phlyctenular keratitis probably of tuberculous origin.

Biopsy of a lesion on the face showed a small focus of tuberculoid structure around a hair follicle.

DISCUSSION OF TWO CASES OF TUBERCULIDS AND ONE CASE OF LICHEN SCROFULOSORUM

DR. LOUIE WINER (by invitation), Minneapolis: The histologic picture in Dr. Stillians' case was definitely typical of lupus miliaris disseminatus because of the infiltrate and central necrosis.

DR. CARL W. LAYMON, Minneapolis: Tuberculids of the papular variety may occur without necrosis. Lupus miliaris disseminatus is an example.

DR. M. J. REUTER, Milwaukee: I think the diagnosis of rosacea-like tuberculid is acceptable in Dr. Stillians' case. The thing that arouses suspicion is the few lesions under the chin, which one does not see in ordinary rosacea.

DR. MICHAEL H. EBERT: I thought the case I presented was interesting in that the cutaneous lesions were associated with tuberculosis of the eyes.

A Case for Diagnosis. Presented by DR. FRANCIS E. SENEAR and DR. HAROLD SHELLOW (by invitation).

L. B., a man aged 42, stated that six years ago an eruption developed on the right cheek, which gradually spread, and later the left cheek became similarly involved. A biopsy performed about five years ago disclosed a sarcoid. For the past four or five years he had been treated with injections of old tuberculin. In January 1942 a tumor started to grow over the left parotid region. It was removed in February after attaining the size of a walnut. He complains of tightness over the precordium, nervousness, dizziness and intermittent pain over the bridge of the nose and left orbit. The eruption consists of pea-sized to bean-sized nodules, many of which have fused to produce plaques on both cheeks. They vary in color from yellowish to bluish red and are firm. Those on the left cheek are harder than those on the right and assume a more raised plaqued appearance, with telangiectatic vessels coursing over them. This area is firmly bound down to the underlying tissue and is painful on pressure. There is accompanying edema of the left infraorbital region.

He has hypertensive heart disease with a blood pressure of 214 systolic and 120 diastolic and a pulse rate of 116. The basal metabolic rate was + 60 per cent. Physical and roentgenographic examinations of the lungs showed no abnormalities. The urine was normal and the Kahn reaction negative. Analysis of the blood showed 80 per cent hemoglobin, 4,750,000 erythrocytes and 7,700 leukocytes, with 21 per cent lymphocytes, 10 per cent monocytes, 67 per cent neutrophils and 2 per cent eosinophils.

Biopsy of an early lesion on the right cheek showed a flattened epidermis, clumping and degeneration of elastic fibers in the upper part of the corium and many sharply outlined nests of cellular infiltrate extending deeply into the corium. These nests intertwined, being separated from each other by normal collagen fibers, and they contained histiocytes, lymphocytes, connective tissue cells and considerable fibrosis.

A section from an older sclerotic lesion on the left cheek showed the entire corium filled by a dense fibrotic infiltrate. A thin layer of clumped elastic fibers persisted just beneath the epidermis. In both sections staining for lipids and for acid-fast bacilli gave negative results.

DISCUSSION

DR. G. A. COOPER (by invitation), Madison, Wis.: I observed a case a year ago in which a lesion appeared resembling the one on the left side of this patient's face. The patient had more adenopathy than this man. During the disease lesions developed on the face which were identical in appearance with this patient's, and she died about a week ago in the leukemic phase with a white blood cell count of 230,000. I think it would be interesting to examine the bone marrow in this case to rule out a lymphoblastoma. Biopsy of bone marrow in my patient established a diagnosis of leukemia.

DR. PAUL A. O'LEARY, Rochester, Minn.: If this man had lesions on only one cheek I should have said the disease was a fibrosarcoma, but the lesions on both cheeks confuse me.

DR. CARL W. LAYMON, Minneapolis: Lesions on both cheeks also confuse me. A fibrotic type of sarcoid must be considered as a diagnostic possibility.

DR. S. W. BECKER: I think the histologic section shows a great deal of collagen. The cells which are overgrowing are connective tissue cells. Fibroma durum is not seen often, but I think the diagnosis would have to rest between fibroma and fibrosarcoma. The clinical picture suggests a foreign body tumor, but there were no signs of vacuoles in the sections.

DR. FRANCIS E. SENEAR: We first saw this man several weeks ago, and for purposes of the record he said that a biopsy had been performed while he was attending the Central Free Dispensary and that at that time he was told that he had sarcoid. Since Dr. Skull is not here, I cannot confirm this.

In regard to Dr. Becker's remarks, I thought of the possibility of foreign body tumor and questioned the patient carefully, but he states that he has had no injections at any time. In attempting to confirm his report on the earlier biopsy we took sections from two different lesions: from the center of one of the large lesions on the left cheek and from an earlier lesion on the right cheek. In neither one was there any suggestion of sarcoid.

Dr. Ebert made a suggestion this afternoon which I think is worth repeating. This patient recalled to his mind one whom Dr. Wile showed about five years ago. That patient had a lesion on the breast which was regarded as a keloid, and it was eventually shown to be a tumor of neural origin. Clinically, if one considers the lesion on the left cheek alone the picture resembles that of the neurogenous lesion of the patient Dr. Wile presented.

Lymphoblastoma Simulating Parapsoriasis. Presented by DR. DAVID KAHN (by invitation).

H. M., aged 72, a retired steel worker of German extraction, presented for Dr. S. W. Becker, entered the clinic in June 1941 with bilateral indurated, painless swelling over the parotid glands of a few months' duration. The left postauricular nodes were enlarged and soft. "Telangiectatic spots" were described as present on the face, head, back and chest. On physical examination the blood pressure was 175 systolic and 90 diastolic. Roentgenotherapy caused regression of the lesions.

In January 1942 a small nodule was noted beneath the anterior border of the left sternocleidomastoid muscle. A month later, this lesion had enlarged to the size of a walnut, and two smaller firm discrete nodes were palpable lower down in this chain. These regressed after roentgenotherapy.

By March 1942 multiple indurated nodules had appeared on the left side of the scalp. Six weeks later, in May, the nodules on the scalp had become larger and more numerous. There was recurrence of the swollen nodes in the left cervical region. Several large (3 by 7 cm. in diameter or larger) circumscribed erythematous telangiectatic macules were present on the chest, back, etc. There was no other peripheral lymphadenopathy. The results of pulmonary, abdominal and neurologic examinations were normal.

The urine was normal. Kolmer and Kahn reactions of the blood serum were negative. The following determinations on the blood were obtained:

	During Eleven Months' Observation	On May 5, 1942
Hemoglobin, per hundred cubic centimeters.....	11.3 to 13.7 Gm.	11.3 Gm.
Erythrocytes	3,500,000 to 4,700,000	4,020,000
Leukocytes	4,200 to 6,300	5,800

Differential counts were within normal limits. Slight anisocytosis with macrocytes was reported.

A roentgenogram of the skull (June 1941) was essentially normal.

Lymphoblastoma. Presented by Dr. S. W. Becker and Dr. S. Rothman (by invitation).

S. C. B., a man aged 44, one and a half years ago, subsequent to a sprain of the right ankle and treatment with a rubber cement cast for six weeks, had erythema and edema of the right foot. One year ago tumors began developing on both legs and nodules appeared in the groins, complicated by an acute suppurative infection of the right foot. The tumors on the leg disappeared after roentgenotherapy. Six weeks ago "red spots" appeared on the hands and diffuse swelling of the right hand developed. At the same time nodules began to appear, particularly on the right arm.

The patient does not feel sick; he is working and he has gained weight during the last year. Nevertheless, he is incapacitated by the pain in the right foot.

Physical examination of the internal organs did not reveal pathologic changes. Examination of the blood showed 4,340,000 erythrocytes, 14 Gm. of hemoglobin and 4,900 leukocytes, with 50 per cent polymorphonuclear leukocytes, 47 per cent small lymphocytes, 2 per cent monocytes and 1 per cent eosinophils.

The cutaneous tumors are globular, blue to violet and sharply limited and firm. There is an extended, rather flatly elevated, sharply circumscribed infiltration with pitting edema on the dorsum of the right hand. Enlarged firm lymph nodes are palpable in the axillas, behind the left ear, in the submandibular region and in the groins. Violaceous and erythematous noninfiltrated spots are irregularly scattered over the arms and legs.

Histologic examination showed intense infiltrate in the deeper layers of the corium. The infiltrate had a rather focal irregular distribution. It was mainly composed of cells which were large and round to oval and had abundant, slightly foamy cytoplasm and large nuclei in which the chromatin was not abundant. The nuclei contained one or more nucleoli. Numerous mitotic figures were seen.

DISCUSSION OF TWO CASES OF LYMPHOBLASTOMA

Dr. Ruben Nomland, Iowa City: I believe Dr. Kahn's patient presents a cutaneous lymphoblastoma of a distinctive type. He has enlargement of several groups of lymph glands but a normal blood count. I have observed 4 fatal cases of this type, and in all the disease ran the same course. There was enlargement of one or several groups of lymph glands for a long time followed by infiltration of the skin with lymphocytes or lymphoblasts. In all cases the blood smear was normal. I suggest calling this patient's condition either a lymphocytic leukemia in an aleukemic stage or lymphocytic lymphosarcoma with specific infiltration of the skin.

Dr. Theodore Cornbleet: The nodules on the scalp in Dr. Kahn's case seemed to be typical of the infiltrative stage of lymphatic leukemia. It is interesting that the blood shows no evidence of leukemia even though there are specific changes present in the skin. Of course, this is well known to happen in some cases.

In the case presented by Drs. Becker and Rothman the lesions on the right hand interest me. They give the impression of numerous sinuses being present

because fluid can be pressed out of the lesion and when the hand is released the expressed fluid can be seen flowing back to its original position. Somebody has suggested the possibility of sarcoma. The presence and appearance of the sinuses and the color of the lesions make me think of Kaposi's sarcoma.

DR. CLARK W. FINNERUD: I did not see the histologic sections. The lesions on the legs were not compatible with Kaposi's sarcoma. I believe the condition will prove to be a true sarcoma.

DR. S. W. BECKER: Dr. Kahn's was presented because of the history of erythematous plaques of several years' duration, and, while there was no scaling and no yellowish discoloration of the lesions characteristic of parapsoriasis, still it showed other features which are characteristic.

The histologic sections are frozen sections and show only that there is a tremendous infiltration of cells of some kind which seem to be more of the lymphocytic type than one would see in Kaposi's sarcoma. The paraffin sections will give more definite information.

NOTE.—Paraffin sections were more suggestive of Kaposi's sarcoma.

A Case for Diagnosis (Pityriasis Rubra Pilaris?). Presented by DR. THEODORE CORNBLEET and DR. D. COHEN (by invitation).

R. G., a white woman aged 56, has had an itching eruption for ten weeks. It began on the face, backs of the hands and feet. There was a rapid generalization after the use of an ointment. The eruption consists of scaling, nonindurated patches and plaques. Elementary lesions forming these patches and plaques appear about the follicles, some of them with keratotic spines. The scalp is thickly covered with a diffuse scaling, and the palms and soles are hyperkeratotic.

The blood and urine were normal, and the Wassermann reaction was negative.

Histologic examination of the section removed was consistent with the diagnosis of pityriasis rubra pilaris.

DISCUSSION

DR. MICHAEL H. EBERT: I should like to ask Dr. O'Leary if this case resembles the ones reported by Brunsting in which there was a vitamin A deficiency with night blindness, which was improved by high doses of vitamin A. Under this treatment the cutaneous lesions improved more slowly, and in 1 case Brunsting was able to demonstrate carotenemia. I think this is a good illustration of the disease that has been classified as pityriasis rubra pilaris which is acquired late in life; it does seem to respond to therapy and disappear. I think that there is good evidence that there is some idiosyncrasy in persons with this condition that prevents them from metabolizing vitamin A properly or makes them require unusually large amounts of this substance, and I think in this case the effect of large doses of vitamin A would be interesting.

DR. PAUL A. O'LEARY, Rochester, Minn.: I believe there are two types of pityriasis rubra pilaris; there are patients with definite night blindness who are helped by vitamin A therapy and those who do not have night blindness, in whom vitamin A deficiency cannot be demonstrated and who are not improved by increase in vitamin A intake. I agree with Dr. Ebert's suggestion, that many of these patients eat a moderate or average amount of vitamin A but for a variety of reasons either do not properly assimilate it or require more of it than the average person. It might well be that the group who do not have a demonstrable vitamin A deficiency do have a deficiency of some other vitamin or combination of vitamins necessary to utilization of vitamin A which has not as yet been recognized.

DR. FREDERICK R. SCHMIDT: I agree with Dr. Ebert in judging this as a case of pityriasis rubra pilaris that comes on later in life. An interesting point I noted in this case is related to a remark made by Dr. Fred Wise. He said that he could diagnose pityriasis rubra pilaris by looking at the back of the patient. By that he meant that there are usually several islands of normal skin so sharply demar-

cated that they stand out from the areas of erythema surrounding them. This is not seen in other cases of erythroderma, and I think it is strikingly shown in this patient.

DR. THEODORE CORNBLEET: Apparently this woman is not now on an abnormal diet. She gets a fairly adequate American diet, but, as the other discussers have stressed, patients with this disease may through imperfect metabolism require what amounts to huge quantities of vitamin A. I cannot help but feel that there must be something more to this group of diseases that improves with vitamin A therapy and yet is not cured than a mere inability to utilize vitamin A properly. It is true that these patients improve sometimes greatly with vitamin A therapy, but there is always some residuum. Why do they not get well if it is only enough vitamin A they lack?

Herpes Zoster of the Geniculate Ganglion with Involvement of the Chorda Tympani and the Motor Fibers of the Facial Nerve. Presented by DR. MICHAEL H. EBERT.

E. F., a white woman aged 45, first noticed twelve days ago a peculiar tingling sensation in the left half of the lower lip. A similar sensation occurred in the left external auditory meatus within the next twenty-four hours. Sensation in the ear gradually increased in severity until it became a dull headache on the left side which was practically constant. A few small blisters were noticed on the lower lip and the anterior two thirds of the left lateral border of the tongue. The region of the left tragus became dull red and edematous and tender, and in a few hours herpetiform blisters appeared. She noticed abnormalities of taste. Two days ago she was first conscious of weakness in the area supplied by the left facial nerve. Pain has been almost continuous from the onset. A few crusted hemorrhagic vesicles are present on the left tragus and at the exitus of the left auditory canal. The area anterior to the tragus is dull red and edematous. The left submaxillary gland is enlarged and tender. There are a few crusted vesicles on the left side of the lower lip just below the vermilion border and a few healing erosions on the left margin of the anterior half of the tongue. There is a definite paresis of the left facial nerve.

DISCUSSION

DR. LEONARD F. WEBER: The thought occurred to me: Why is paresis not seen more often with zerpes zoster?

DR. HERBERT RATTNER: There was a similar patient here at the hospital six months ago. Such a condition is not common and is referred to in the literature as the Ramsey Hunt syndrome. The patient recovered from his paresis, but, as I recall it, only after considerable time had elapsed.

DR. MICHAEL H. EBERT: This patient is a physician. It is my impression that herpes zoster of the geniculate ganglion is relatively rare. This syndrome was first described by an otolaryngologist, Dr. Hunt. It can be confusing. The first symptom is extreme pain in the ear, and the patient is seen almost always by the otolaryngologist first. The drum is apparently normal or slightly erythematous, and examinations are made to see if there is involvement of the mastoid processes. After a few days a slight herpes develops, and that eruption was described by Hunt as involving an area which started at the depth of the auditory canal and extended to the aperture of the canal and the areas around the aperture, but without much more extension. The geniculate ganglion is a sensory ganglion on the facial nerve. When it is involved the motor branches of the facial nerve are often involved. Consequently facial paresis is often associated. The eighth nerve is also frequently involved but was not in this case. When such involvement occurs there may be tinnitus, dizziness, deafness, and even nausea and vomiting. I have observed only 1 such case, that of an elderly woman with high blood pressure in whom the disease was diagnosed as hemiplegia. In my case the chorda tympani was involved at first, but today one can see only a few relics on the tongue.

The little group of herpes lesions on the lower lip probably represents an aberrant sensory branch of the facial nerve.

Unilateral Erythema Nodosum. Presented by Dr. David Kahn (by invitation).

N. S., a woman aged 20, a typist, presented for Dr. S. W. Becker, fractured her left ankle in June 1939. Three months later her left leg "felt sore" and then small "lumps" appeared. These lesions were painful and red at first, later resembling a bruise with tenderness. Despite remissions, more lesions have gradually appeared. Three months ago a tonsillectomy was performed with a resulting exacerbation, at which time a transient lesion appeared below the right knee for the first and only time. The lesions on the left extremity have spread to involve the thigh during the past few months.

The patient has noted headaches since last summer. She has occasional head colds and frequent sore throat. There are no pulmonary complaints or loss in weight. A questionable history of contact with tuberculosis in a friend was obtained.

Examination of the skin revealed livid and blue-black nodules of varying size, extending from the left ankle to the hip anteriorly and laterally. The whole leg, particularly the nodules, is tender to pressure.

Physical examination revealed a mucopurulent nasal and postnasal discharge, mild pyorrhea, a soft systolic murmur at the cardiac apex and a few rales at the base of the left lung.

Fluoroscopy of the chest showed it to be normal. A tuberculin test with a dilution of 1:1,000,000 elicited a negative reaction on two occasions. The urine was normal. Kolmer and Kahn reactions of the serum were negative. The sedimentation rate in one-half hour was 6 mm. and in one hour 14 mm.

DISCUSSION

Dr. E. A. Oliver: I have seen the patient several times and have never been able to understand the case. The lesions are at times of erythema nodosum type, but I have never before seen this disease affect one side of the body only. At one time she did have a few lesions on the right leg, but most of the eruption has been confined to the left leg and thigh. She has had foci of infection removed. At one time I thought that she might have a dermatitis factitia, but the lesions are so typical of erythema nodosum that I do not believe it is possible for her to have produced them.

Dr. S. W. Becker: I felt as Dr. Oliver did, that dermatitis factitia must be considered. I have never seen anything like this eruption before. The lesions are typical of erythema nodosum on the leg, but on the thigh they are somewhat different. She had a fracture of this leg some years ago, which is the only point in the history that might predispose to unilateral involvement. When her tonsils were taken out she had a few lesions on the other leg. I asked her if she had been pounding herself with a hammer, and she stated that she had not. The biopsy showed typical erythema nodosum. I cannot account for the unilateral involvement unless something happened when she fractured her leg.

Pityriasis Lichenoides Chronica Varicelliformis. Presented by Dr. Maurice Oppenheim (by invitation) and Dr. D. Cohen (by invitation).

H. P., a white woman aged 25, presents a disseminated eruption which has been present about one year and is not pruritic. The eruption is polymorphous, consisting of macules and papules. On her first visit many papules presented central crusts. The first impression was chickenpox. The entire body is involved with the exception of the face and scalp, the trunk less than the extremities and the extensor surfaces of the extremities more than the flexor. The color varies from yellow-red to brownish red. The size varies from that of a pinhead to that of a finger nail. Some of the borders are sharp and others are not. The surface

shows few flakelike scales or crusts. Under diascopic pressure a yellowish color persists. The disease seems to start with a papule, which later become flatter and forms in the later stages macules with fine wrinkled surfaces simulating superficial atrophy. The mucous membranes are not involved.

The Kahn reaction was negative on two occasions. The urine and blood were normal. A roentgenogram of the chest did not show evidence of tuberculosis. The Pirquet test elicited a 4 plus positive reaction, raised and over the size of a nickel, and the Mantoux test a 3 plus positive reaction.

Histologic examination showed round cell infiltration in the cutis and subcutis around the blood vessels. The subpapillary blood vessels were enlarged. There was a slight degree of edema in the papillary and subpapillary layer. The border between the papillary layer of the cutis and the epidermis was not sharp and in some areas not visible. There was some transmigration of leukocytes into the epidermis. Parakeratotic areas were seen.

DISCUSSION

DR. HERBERT RATTNER: I should like to raise a point of terminology. I am familiar with the names pityriasis lichenoides chronica and pityriasis lichenoides et varioliformis acuta, but not the name used in this case.

DR. MAURICE OPPENHEIM (by invitation): This is a term which was used in Vienna by myself the first time. In this case the first impression was chickenpox. The condition at that time was not at all like it is today, but one can still see papules with central superficial necrosis. There is no doubt that there is present also now a typical picture of pityriasis lichenoides chronica varicelliformis. This condition has some relation to tuberculosis in my belief.

News and Comment

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY

The next meeting and examination of the American Board of Dermatology and Syphilology will be held in Philadelphia on Friday and Saturday, Nov. 5 and 6, 1943.

The written examination will be held in various large cities on Monday, Sept. 27, 1943.

Applications for this examination must be filed in the secretary's office by Aug. 16, 1943.

C. GUY LANE, M.D., Secretary,
416 Marlborough Street, Boston.

DEATHS

Dr. J. Frank Fraser died on Jan. 31, 1943, in New York.